



# SURGERY

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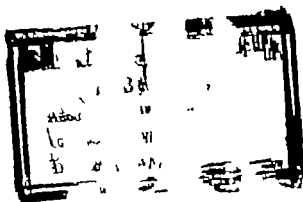
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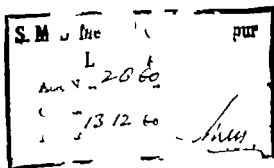
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# SURGERY

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No. 1

## Original Communications

### RESECTION OF THORACIC ESOPHAGUS FOR CARCINOMA LOCATED ABOVE ARCH OF AORTA. CERVICAL ESOPHAGOGASTROSTOMY

JOHN H. GARLOCK, M.D., NEW YORK, N. Y.

(From the Surgical Service, Mount Sinai Hospital)

IT IS fortunate that the least frequent site for cancer to attack the esophagus is that portion of the organ located between the superior border of the aortic arch and the apex of the chest or root of the neck, an area termed the superior mediastinum. It has been known for many years that this portion of the esophagus is difficult to approach surgically. It will be remembered that at this location, the esophagus lies posterior and to the left of the trachea, and medial to the left great vessels, and is in close proximity to both vagus and recurrent laryngeal nerves. The thoracic duct begins to swing outward to the left and is not in as close contact with the esophagus as it is behind the arch of the aorta. Many years ago Ziaja, Kuttner, and Gauerbruch attempted to excise carcinomas of the esophagus in this location by utilizing an anterior approach splitting the clavicle and upper ribs. Although the exposure was adequate it was unnecessarily mutilating and the operation was never completed from the standpoint of re-establishing gastrointestinal continuity.

Unfortunately tumors in this location are all too frequently locally inoperable when the patients first consult the surgeon. A tumor growing in a peripheral direction will soon involve the left recurrent laryngeal nerve, vagus nerve, or trachea. There may be extensive involvement of the cervical lymph nodes. It has been our experience that local inoperability is found more frequently with tumors in this location than with any other portion of the organ. Therefore the opportunity to carry out a radical resection will be infrequent. Still the surgeon should have at his command an operative procedure which can be utilized for the infrequently operable case and which embodies all the recently developed concepts of the rational surgical treatment of malignancy of other portions of the esophagus. It is for this reason that I would like to describe an operative procedure that was utilized to excise a large intraluminal fungating tumor in this location with re-establishment of esophagogastric continuity by uniting the transplanted stomach to the remains of the esophagus in the neck.

Received for publication, May 17, 1947



It seems unnecessary to stress the fact that the surgeon should use every expedient to determine operability before subjecting the patient to exploration. Preoperative studies should include careful chest roentgenograms, laryngeal examination to disclose left recurrent nerve involvement, bronchoscopy to indicate tracheal infiltration and respiratory studies to exclude vagus nerve invasion. Palpatory examination of the neck will indicate the presence or absence of metastatic nodes. If any of the mentioned structures are found to be definitely invaded by the growth, exploration should not be undertaken.

From the standpoint of disturbed physiology a very operative manipulation on the esophagus in this location especially if the tumor is a large one and extends toward the right side of the mediastinum has one dangerous feature which the surgeon must appreciate thoroughly. I refer to the inadvertent stimulation of both vagus nerves in their suprasternal location, something which the surgeon may find impossible to avoid if he is to remove completely the tumor-bearing part of the esophagus. Such stimulation may set up the so-called vagovagal reflex which may result in irreversible disturbances of cardiac function and cause death of the patient. This is what I believe happened to the patient reported in this paper. Whether thorough preoperative and peroperative atropinization will prevent this serious complication remains to be seen. My physiologist friends tell me that atropine should be good insurance against this eventuality. Further experience is needed to settle this point.

#### CASE REPORT

Mrs. D. B. (Hospital No. 538563) aged 48 years was admitted to Mount Sinai Hospital on Dec. 24, 1946, complaining of dysphagia of three months' duration. The dysphagia originally noted when swallowing solid food and was accompanied by substernal pain radiated to the upper sternal region. At the time of admission, the patient was able to swallow only liquids. There had been a loss of fifteen pounds. The past and personal histories were negative. Her mother had died of carcinoma of the stomach.

**Physical Examination.**—Examination indicated rather obese woman not appearing ill. There was nothing abnormal to be felt in the neck. Heart findings were negative; pulse 88, bloods and pelvic findings were negative. Blood pressure was systolic 130 mm. diastolic 90 mm.

**Laboratory Work-up.**—Laboratory studies showed hemoglobin 108 per cent, white blood cells 12,000 (in normal differential). Electrocardiogram was negative. X-ray examination of the chest showed negative results. Roentgenographic examination of the esophagus showed a large irregular mass which partially obstructed the esophagus at the upper level of the aortic arch.

**Esophagoscopy.**—At 18 cm. from the upper incisor teeth, found a large irregular grayish mass which, on biopsy proved to be an infiltrating hemorrhagic squamous cell carcinoma.

**Total Capacity.**—Total capacity was found to be 2.4 liters, or 74 per cent.

**Preoperative.**—Preoperative preparation consisted of high caloric fluid intake, parenteral vitamins, arterial puncture cannulization of trachea and bronchi for 10 days, and no chemical clearing of the esophagus through Levine tube.

**Operation.**—Operation was done Jan. 3, 1947, under intratracheal gas-oxygen-ether anesthesia. The patient was placed on the operating table in such a position as to incline the left side upward and somewhat toward the table exposing simultaneously the upper abdomen.

thorax, and neck. This entire area prepared and draped for simultaneous accessibility to chest and neck. An oblique incision was made along the left sternomastoid muscle. By retracting the left lobe of the thyroid access was gained to the posterior mediastinum. By blunt finger dissection, the superior mediastinum was palpated. The upper half of the tumor could be delineated in this case and it was decided that the tumor was resectable. The cervical wound was then closed temporarily.

*Thoracic Stage*—A long incision was made over the left seventh rib which was removed subperiosteally (Fig. 1). A widely opened rib spreader gave excellent exposure of the entire left side of the chest. The mediastinal pleura was then moved back and below the aortic arch. There was disclosed a large tumor of the esophagus starting about the level of the middle of the arch and extending posteriorly to a point about one inch below the arch. The tumor projected more into the lumen than toward the periphery of the organ and extended

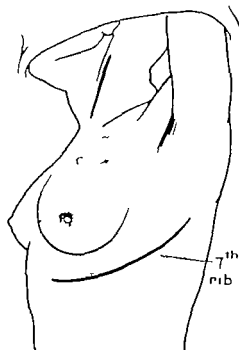


Fig. 1.—Diagrammatic sketch showing thoracic incision over the seventh rib which is removed subperiosteally.

to the right side of the mediastinum. It measured about 10 inches in its transverse diameter. After great deal of difficulty it was dissected free from surrounding structures. During this process, the left vagus and recurrent nerves and the thoracic duct were visualized and protected. The right nerves were never seen. The phrenic nerve was pinched to immobilize the left leaf of the diaphragm. The latter structure was then incised radially from the esophageal hiatus outward. The cardiac end of the stomach freed from the diaphragm and the whole stomach was mobilized by ligating and dividing the vasa brevia, the left gastroepiploic vessels and left gastric artery to its origin from the celiac axis. The gastrocolic ligament on left attached to the stomach to preserve the entire gastroepiploic arch. The stomach was thus freed as if the pylorus. No enlarged lymph nodes were found.

It seems unnecessary to stress the fact that the surgeon should use every expedient to determine operability before subjecting the patient to exploration. Preoperative studies should include careful chest roentgenograms, laryngeal examination to disclose left recurrent nerve involvement, bronchoscopy to indicate tracheal infiltration and circulatory studies to exclude vagus nerve invasion. Palpatory examination of the neck will indicate the presence or absence of metastatic nodes. If any of the mentioned structures are found to be definitely invaded by the growth, exploration should not be undertaken.

From the standpoint of disturbed physiology any operative manipulation on the esophagus in this location, especially if the tumor is a large one and extend toward the right side of the mediastinum has one dangerous feature which the surgeon must appreciate thoroughly. I refer to the inadvertent stimulation of both vagus nerves in their suprasternal location something which the surgeon may find impossible to avoid if he is to remove completely the tumor-bearing part of the esophagus. Such stimulation may set up the so-called vagovagal reflex which may result in irreparable disturbances of cardiac function and cause death of the patient. This is what I believe happened to the patient reported in this paper. While the thorough preoperative and operative atropinization will prevent this serious complication remains to be seen. My physiologist friend tell me that atropine should be good insurance against this eventuality. Further experience is needed to settle this point.

#### CASE REPORT

Mrs. D. B. (Hospital No. 553285) aged 46 years, was admitted to Mount Sinai Hospital on Dec. 4, 1946, complaining of dysphagia of three months duration. The dysphagia originally was noted when swallowing solid food and was accompanied by substernal pain radiating to the upper sternal region. At the time of admission, the patient was able to swallow only liquids. There had been loss of fifteen pounds. The past and personal histories are negative. Her mother had died of carcinoma of the uterus.

**Physical Examination.**—Examination indicated nothing abnormal except pressing all there was nothing abnormal. He felt in the neck. Heart findings were negative. pulse 64, blood pressure and petri had negative. Blood pressure was systolic 120 mm. diastolic 80 mm.

**Laboratory Work.**—Laboratory studies showed hemoglobin 100 per cent with blood cells 1,540 with normal differential. Electrocardiogram was negative. X-ray examination of the barium swallow (see fig. 1) result. Roentgenographic examination of the esophagus showed large irregular mass which partially obstructed the esophagus at the upper level of the aortic arch.

**Esophagoscopy.**—At 14 cm. from the upper incisor teeth was found large irregular grayish tumor which, on biopsy proved to be an infiltrating keratinizing squamous cell carcinoma.

**Vital Capacity.**—Vital capacity was found to be 4 liters, or 74 per cent.

**Preoperative Preparation.**—Preoperative preparation consisted of high barium swallow, peroral fluoroscopic examination of trachea and bronchi for at least 4 days, and mechanical clearing of the esophagus through Levine tube.

**Operation.**—Operation was done Jan. 2, 1947 under intratracheal gas-oxygen ether anesthesia. The patient was placed on the operating table in such way as to incline the left side toward the head of the table exposing simultaneously the upper abdomen.



The esophagus was divided at the cardiac junction and the opening in the stomach closed with three layers of silk sutures (Fig 3). The mobilized esophagus was brought up from behind the arch of the aorta so as to lie in a completely supra-arterial position. The neck wound was then reopened and the mobilized thoracic esophagus was brought out of the neck wound, care being taken not to compromise the esophageal branches of the inferior thyroid artery. The neck vessels were covered temporarily and the thoracic part of the operation was then completed. The mobilized stomach was brought to the apex of the chest. It was found that the upper three inches of the organ could be pushed through the apex of the chest into the neck without any tension whatsoever and without demonstrable interference of blood supply. To

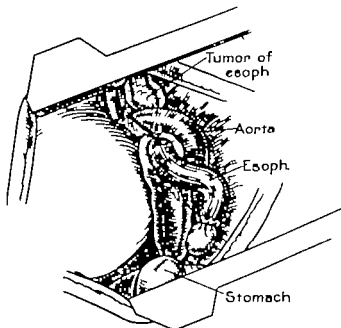


Fig 3.—The esophagus has been mobilized, no radial incision made in the left half of the diaphragm. Transection was done at cardioesophageal junction with double inversion of the cardia and mobilization of tumor-bearing portion of esophagus above arch of aorta.

guide sutures of silk were then placed in the wall of the stomach to be utilized for the same purpose and these were withdrawn from the neck wound, thus helping to apply the proper amount of tension on the transplanted stomach (Fig 4). The latter was anchored in new position by a series of silk sutures between stomach and both edges of the mediastinal pleura (Fig 4). The diaphragm was repaired around the transplanted stomach. A rubber tube placed in the neck interspace for suction or drainage and the chest wound closed in layers.

**Cervical Stage.**—The patient was turned on the back and the neck wound was reopened. The esophagus was divided well above the tumor and the cardiac portion of the stomach identified by the guide sutures was approximated the esophageal stump (Fig 5). The usual two-layer interrupted silk suture anastomosis then effected (Fig 6). The stomach was anchored to neighboring areolar tissue in the base of the neck to prevent any drag on the anastomosis. Goss padding was inserted to obliterate the opening in the pleural space and the neck was closed around it (Fig 7).

During the course of the operation, which lasted four and one-half hours, the patient was given 1,500 cc of whole blood. At the end of the blood pressure was systolic 110 and

diastolic 70, with a pulse of 110. At the end of the operation the systolic pressure was 80 and the diastolic 40. The pulse was 110. The graph of the blood pressure and pulse maintained remarkably even line. At 9:45 p.m. pulse was 100; at 10:10 p.m. pulse 80, blood pressure 170/70. At 10:45 p.m. pulse 102, respiration coefficient at 13 r.m. pulse 80, blood pressure 105/64. At 12 midnight, pulse 100. At 6 a.m. pulse 100. At no time was there any evidence of shock. Late in the morning the patient developed marked cyanosis accompanied by respiratory distress and died very quickly.

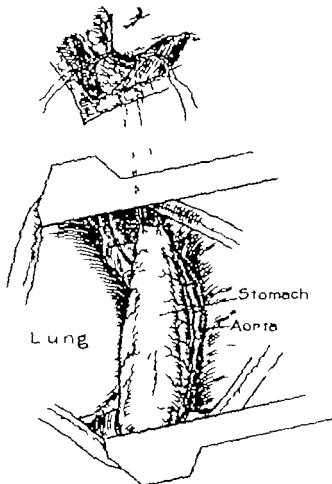


Fig. 2.—The stomach has been mobilized as far as the pylorus leaving intact the gastro-epiploic vessels. The guide sutures placed in the cardiac region are being pulled through the neck incision.

A complete post-mortem examination did not reveal any cause of death. The main bronchus intact and the blood supply of the stomach in its new position was excellent. It is believed that the patient's death was caused by profound pathologic disturbance possibly caused by vagal stimulation.

#### COMMENT

The operation reported in this paper seems a natural sequence of the operation I described two years ago for carcinomas of the middle third of the esophagus with esophagogastric anastomosis above the arch of the aorta. I do not

The esophagus was divided at the cardiac junction and the opening in the stomach closed with 4 layers of silk suture (Fig. 2). The mobilized esophagus was brought up from behind the arch of the aorta so as to lie in a completely supra-ortic position. The neck wound was then reopened and the mobilized thoracic esophagus was brought out of the neck wound, care being taken not to compromise the esophageal branches of the inferior thyroid artery. The neck artery was covered temporarily and the thoracic part of the operation was then completed. The mobilized stomach was brought to the top of the chest. It was found that the upper three inches of the organ could be pushed through the top of the chest into the neck without any tension whatsoever and without demonstrable interference of blood supply. To

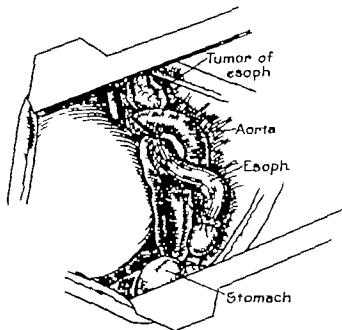


FIG. 2.—The esophagus has been mobilized and radial incision made in the left leaf of the diaphragm. Transference is done (cardioesophageal junction) with double inversion of the cardia and mobilization of tumor-bearing portion of esophagus below arch of aorta.

guide sutures of silk were then placed in the end of the stomach to be utilized for the anastomosis and these were withdrawn from the neck wound, thus helping to pop the proper amount of tension on the transplanted stomach (Fig. 3). The latter was anchored in its new position by a series of silk sutures between stomach and both edges of the mediastinal pleura (Fig. 4). The diaphragm was repaired around the transplanted stomach. A rubber tube placed in the sixth interspace for suction or drainage and the chest closed by four layers.

**Critical Stage.**—The patient was turned on the back and the neck wound was reopened. The esophagus was divided well below the tumor and the cardinal portion of the stomach mobilized by the guide sutures was approximated the esophageal stump with care (Fig. 5). The usual two-layer interrupted silk suture anastomosis as is effected (Fig. 6). The anastomosis to neighboring areolar tissue in the lower part of the neck to prevent any

diastolic 70 with pulse  $f$  110. At the end of the operation the systolic pressure was 80 and the diastolic 40. The pulse was 110. The graph of the blood pressure and pulse maintained remarkably even line. At 9:45 P.M. pulse was 100 at 10 P.M. pulse 80, blood pressure 120/70; at 10:45 P.M. pulse 102, condition excellent; at 11 P.M. pulse 96, blood pressure 102/64; at 12 midnight pulse 108; at 6 A.M. pulse 100. At no time was there any evidence of shock. Later in the morning the patient developed marked cyanosis accompanied by respiratory distress and died very quickly.

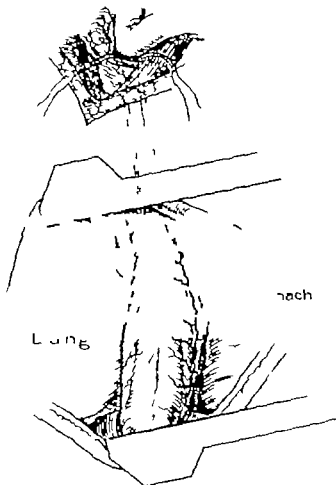


Fig. 3.—The stomach has been mobilized as far as the pylorus being intact the gastro-jejunal reflux. The guide sutures placed in the cardiac region are being pulled through the neck incision.

A complete post-mortem examination did not reveal any cause of death. The stomach was intact and the blood supply of the stomach in its new position was excellent. It is believed that the patient's death was caused by profound physiologic disturbances, possibly caused by vagal stimulation.

#### COMMENT

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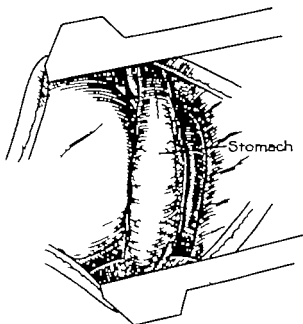


Fig 4—After sufficient stomach has been withdrawn through the lower angle of the neck incision, the stomach is now fixed to the left edge of the mediastinal pleura and the opening in the diaphragm is being repaired around the transplanted stomach.

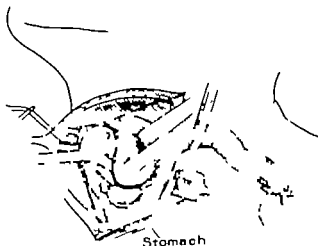


Fig 5—This diagram indicates the upper end of the stomach in the low angle of the incision being approximated to the diaphragm.

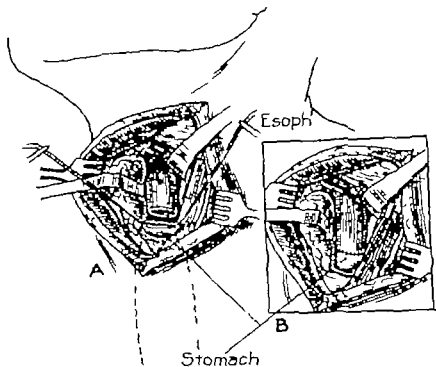


Fig 6.—The tumor-bearing portion of the esophagus has been removed and an end-to-side anastomosis effected between the stump of the esophagus and the stomach, using 12 layers of interrupted silk sutures.

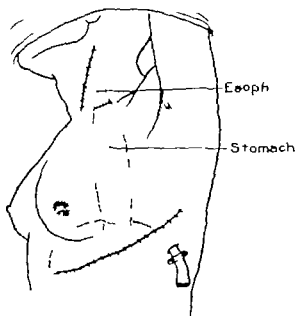


Fig 7.—Diagrammatic sketch showing the transplant line of the stomach through the chest into the lower cervical region. Its anastomosis of the stomach to the esophagus.

believe that there is a very increased danger to the blood supply of the stomach by bringing part of the organ into the neck through the superior aperture of the thorax. This case demonstrates that, in the patient of average height, the stomach can be mobilized sufficiently to permit its transplantation above the apex of the chest without impairment of its vitality. The blood supply of the stump of the esophagus in the neck can be assured by preservation of the esophageal branches of the inferior thyroid artery. If on further trial this operation proves to be feasible it will be unnecessary to employ the multiple procedures needed for transplantation of a loop of jejunum to bridge the defect between stomach and neck. This operation originally described by Lexer years ago, has been recently revived by the Russian surgeon Yudin, Longmire and others. These procedures are fraught with considerable danger first, from the standpoint of vitality of the transplanted jejunum second from the standpoint of healing between stomach and jejunum and esophagus and jejunum with the ever present risk of fistula formation, and finally because of the real danger of stricture at the two sites of anastomosis. To overcome the first difficulty Longmire recently advocated a direct anastomosis between the internal mammary artery and the mesenteric vessels of the loop of jejunum. The use of the stomach as herewith reported would make all of these maneuvers completely unnecessary. It is probable that this operation could be utilized also for extensive impermeable lye strictures of the thoracic esophagus the same way as Sweet employed the supra-aortic anastomosis of a lye stricture of the middle third of the organ. If this operation proves to be feasible all of our problems concerned with malig-  
 nancy of various segments of the esophagus will be greatly simplified. Only by a process of trial and error can we arrive at a common denominator for the successful surgical therapy of this disease.

## COMBINED LEFT ABDOMINAL AND RIGHT THORACIC APPROACH TO RESECTION OF ESOPHAGEAL NEOPLASMS

JOSEPH B. MACMANIS M.D. BUFFALO, N. Y.

(From the Rosell Park Institute for Malignant Disease and the University of Buffalo Medical School)

**D**URING the four years from 1944 to 1948 increasing success has been experienced in the resection of neoplastic lesions of the esophagus with re-establishment of the continuity of the intestinal tract. Many factors have been responsible for this: (1) The development and administration of anesthetics by highly trained medical personnel acutely aware of the physiological abnormalities created by the open thorax. (2) the better understanding by those preparing these patients for surgery of the importance not only of nutritional factors such as protein and vitamin replacement but also of restoring depleted blood volumes, by transfusion before the patient arrives at surgery. (3) the proper use of the antibiotics. (4) the use of large volumes of blood during surgery. (5) the increased knowledge of thoracic surgery and the appreciation of those practices in operative technique and postoperative care which prevent or at least minimize many of the complications of this type of surgery.

Many operative approaches have been used in the resection of lesions of the middle and lower esophagus with the purpose of performing a complete cancer operation as was feasible and yet by re-establishing the continuity of the intestinal tract provide for at least palliation should a cure not be possible. The left transthoracic approach and the thoraco-abdominal incisions used by Sweet and Garlock for the lower esophagus have perhaps been the best outlined in the recent literature.

There are a few very outstanding disadvantages, however to the conventional approaches through the left thorax whether they be purely transthoracic or include an extension through the costal arch into and through the abdominal parietes. If the transthoracic approach has been used without a preliminary abdominal exploration the perator may subject the patient to a major procedure only to find after the thorax and the diaphragm have been opened that the lesion has already involved the liver. Again when resecting lesions in the lower third of the esophagus one frequently has a tendency to divide the esophagus on the cephalad side much too close to the neoplastic process because for each higher level of transection the subsequent anastomosis becomes increasingly difficult to perform technically and one reaches a level about the seventh dorsal vertebra where the esophagus had better be passed behind the arch of the aorta and anastomosed anteriorly to it to complete the anastomosis. This additional amount of surgery does increase the mortality of the procedure perhaps at least partially because of disturbed pulmonary and cardiac reflexes resulting from unsplashed trauma

believe that there is any increased danger to the blood supply of the stomach by bringing part of the organ into the neck through the superior aperture of the thorax. This case demonstrates that in the patient of average height, the stomach can be mobilized sufficiently to permit its transplantation above the apex of the chest without impairment of its vitality. The blood supply of the stump of the esophagus in the neck can be assured by preservation of the esophageal branches of the inferior thyroid artery. If on further trial this operation proves to be feasible, it will be unnecessary to employ the multiple procedures needed for transplantation of a loop of jejunum to bridge the defect between stomach and neck. This operation originally described by Lexer years ago, has been recently revived by the Russian surgeon Yudin, Longmire and others. These procedures are fraught with considerable danger: first, from the standpoint of vitality of the transplanted jejunum; second, from the standpoint of healing between stomach and jejunum and esophagus and jejunum with the ever present risk of fistula formation, and finally because of the real danger of stricture at the two sites of anastomosis. To overcome the first difficulty Longmire recently advocated direct anastomosis between the internal mammary artery and the mesenteric vessel of the loop of jejunum. The use of the stomach as herewith reported would make all of these maneuvers completely unnecessary. It is probable that this operation could be utilized also for extensive impermeable strictures of the thoracic esophagus in the same way as Sweet employed the supra-aortic anastomosis for dilatation of the middle third of the organ. If this operation proves to be feasible all of our problems concerned with malignancy of various segments of the esophagus will be greatly simplified. Only by a process of trial and error can we arrive at a common denominator in the successful surgical therapy of this disease.

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There are a few very outstanding disadvantages, however to the conventional approaches through the left thorax whether they be purely transthoracic or include an extension through the costal arch into and through the abdominal parietes. If the transthoracic approach has been used without a preliminary abdominal exploration, the operator may subject the patient to a major procedure only to find after the thorax and the diaphragm have been opened that the lesion has already involved the liver. Again when meeting lesions in the lower third of the esophagus, one frequently has a tendency to divide the esophagus on the cephalad side much too close to the neoplastic process because for each higher level of transection the subsequent anastomosis becomes increasingly difficult to perform technically and one reaches a level about the seventh dorsal vertebra where the esophagus had better be passed behind the arch of the aorta and carried anteriorly to it to complete the anastomosis. This additional amount of surgery does increase the mortality of the procedure perhaps at least partially because of disturbed pulmonary and cardiac reflexes resulting from unavailability of

to the mediastinal nerve plexuses and from reflexes arising from the aortic arch which must be partially mobilized to effect the transfer of the esophagus anteriorly. In our earlier cases, perhaps for this reason, transection was, on occasion, too close to the gross lesion. Sections taken through the transected margin of some of these have shown neoplastic cells in the submucosa. This of course has been noted by many others.

A third factor which becomes of some importance in middle third lesions bear comment. It is not uncommon to find the lesion adherent to the right mediastinal pleural reflection. At the lower border of the fourth dorsal vertebra the azygos vein arches forward across the esophagus to drain into the superior vena cava. Lesions which are adherent to this larger vein when approached through the left side of the chest beneath the lung root are technically very difficult and hazardous to remove without the constant danger of serious bleeding even when the opposite (right) side of the thorax is deliberately opened to facilitate this dissection. When operating through the left side of the chest the diaphragm of course must be opened widely. In so doing if one does not crush the phrenic nerve one cuts across most of its branches near the hiatus which serves to make it functionless for many months and in some cases permanently. The quiet diaphragm is helpful during the operative procedure, but postoperatively this state is believed to be a decided advantage. Its abnormal position makes it difficult to detect supra- and infradiaphragmatic collections of fluid in the costophrenic angles on this side. It favors the development of atelectasis in the lower lobe with perhaps, at times, permanent crippling of this lobe through formation of adhesions between the collapsed lobe and the intrathoracic stomach. (The early stages of this pathology have been seen in one case at autopsy.) Perhaps the most serious physiologic effect is the loss of tufting power. In a small series of fourteen completed resection done through the left side of the thorax the incidence of patchy areas of pneumonia has been large (over 50 per cent). The problem of urging and stimulating these patients to cough effectively postoperatively has been a real one and some of this difficulty doubtless is due to the loss of tufting power attending complete paralysis of the left half of the diaphragm.

In an effort to avoid many of these difficulties two extra dissections were undertaken with the purpose of eliminating the disadvantages and feasibility of a combined approach, using a left upper lobotomy and a right thoracotomy approach through the bed of the seventh rib. In the dissections it was found necessary to divide the right crus of the diaphragm posterior to the position of the right phrenic nerve on the diaphragm. Otherwise the technique used was identical to one published by Ivo Lewis in 1946. This combined approach was carried out on six patients and it was surprising to observe that the operation seemed technically less tedious, maintained its status as a cancer operation, preserved the phrenic nerve function bilaterally, did not require radical incisions in the diaphragm, allowed one to transect

the esophagus at any desired level and effect an anastomosis without interference with the aortic arch resulted in less total gross trauma to the patient's tissues, and consumed less operating time. Postoperatively the tissue power was well preserved in both patients.

One cannot develop a thesis in this case and such is definitely not intended. Nor is this approach presented as an original contribution for Ivor Lewis, the British surgeon, has already reported on its use in an earlier periodical. A description is offered of the conduct of the operation in the hope that others may use it and report on both its advantages and disadvantages and so perhaps help to clarify the status of the procedure.

*Indications for the Use of the Combined Approach*—The combined approach will probably find its greatest usefulness in the resection of lesions of the middle third and lower third when the lesion does not involve the crura of the diaphragm. A leiomyosarcoma of the cardia of the stomach with extension into the esophagus and with possible infiltrations into the left leaf of the diaphragm may be difficult if not impossible to remove safely through this combined approach.

*Conduct of the Operation*—The operation is divided into two stages. These may be done consecutively on the same day or separated by an interval of seven to ten days. It is preferable of course to complete the operations on the same day.

*First stage*—An incision is made just to the left of the midline beginning at the xiphoid and extending below the umbilicus. The rectus muscle is split and the peritoneum opened. The peritoneal cavity is explored for evidences of metastases, particular attention being given to the liver, pre-aortic and paraesophagocardiac nodes, and the lymph nodes near the hilum of the spleen. Patients who present metastases to the liver are not considered suitable subjects for the complete resection. The gastrosplenic ligament is taken down, the level of section being a few centimeters from the border of the right gastroepiploic artery. The individual vessels are secured with fine silk, and the dissection and ligation are carried around the greater curvature of the stomach dividing the left gastroepiploic artery and the vasa brevia passing to the spleen. The stomach is then turned upward and the left gastric artery doubly ligated as close to its origin as possible thus leaving behind a sheath of vessels which may serve as collateral channels for blood being delivered from the right gastric artery. If large nodes are present about these vessels they will of course have to be resected with the specimen later in the procedure. The gastrophrenic mesentery is then ligated to the diaphragm. If the left lobe of the liver obscures the field it is mobilized from the diaphragm by dividing the left suspensory ligament. This ligament is usually relatively avascular. The liver can then be retracted upward and free access to the esophagocardiac junction obtained. The peritoneal reflection from the diaphragm over the esophagus is severed after the anastomotic vessels which one commonly find beneath this reflection are ligated. It is advisable to use silk thread for all sutures borne to allow a unit time lapse between



stages less reaction can be expected and therefore less likelihood of adhesion formation sufficient to interfere with delivery of the stomach into the chest. At this point the technique differs from that of Lewis. A point has been made of dividing the right crus of the diaphragm near its origin. It is felt that this division not only makes the blunt dissection from below of the lower two inches of the mediastinum easier but it allows one a larger space through which to maneuver the stomach during the third stage of the operation. The diaphragm is also less likely to act as a partial obstruction to the vagotomized stomach at some later date. However there are certain precautions to follow in dividing the crus which it may be worth while to mention. The origin of the thoracic duct from the external chyl

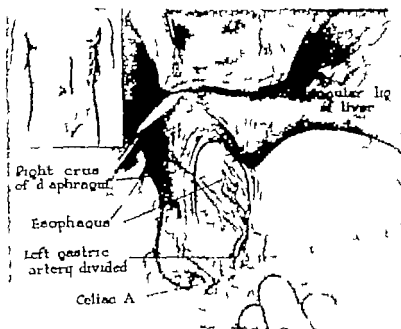


Fig. 1—First stage (hiatal approach). The incision shows the peritoneal reflection of the stomach and the abdominal aorta. The large incision indicates the approximate location of the division of the right crus after the stomach has been mobilized in preparation for its entry into the chest at the second stage.

takes place behind the right crus of the diaphragm and it should be noted in cutting the muscle fibers so as not to injure this important structure. If blunt dissection is used on the cephalic surface of the crus, the soft tissues may be peeled away easily exposing the muscle fibers of the crus well back from its margin. The right inferior phrenic artery and its branches usually lie well back of the margin of the right crus but since the position is variable troublesome bleeding may occur when the crus is lifted. Better ligatures placed before the division is carried out may avoid an emergency in this sort. When the esophagus has been freed from the mediastinum of

a distance of approximately two inches, the abdomen is closed. At this point a jejunostomy may be done for feeding purposes if the operator so desires to conduct the case. Fortunately in this reported series of twenty-one cases, patients in the large majority of instances could swallow liquids if given slowly and they had been prepared adequately by a high calorie fluid diet supplemented by drip feedings during the sleeping hours. For this reason there were not frequent occasions to use jejunostomy in preparation for resection. The closing of the abdomen completes the first stage. This procedure is attended by very little blood loss.

*Second stage* The patient is turned over on the left side the skin prepared, and the region about the seventh rib draped. Whether one selects the fifth, sixth, seventh or eighth ribs depends a good deal on the level of the lesion as well as the height of the diaphragm. In general, that rib is selected whose neck is on a level two vertebrae above the upper border of the lesion as determined by x-ray examination. This, of course is not accurate as the actual extent of the lesion may in some cases far exceed the apparent extension as determined by the roentgenologist. We can however transect the ribs above and below the resected one for further exposure as the case requires. The thorax is opened through the bed of the selected rib. The right lung is then gently decompressed and packed off medially. It may not be necessary to ligate and divide the axillary vein in lower third lesions but in all other cases it seems advisable. The mediastinal pleura is opened from a point three inches above the lesion down to the diaphragm and resectability is determined. Three types of local conditions have prevented resections in our hands. They are invasions of (1) the lung root, (2) the vertebral bodies, and (3) the aorta. When lesions lie behind the arch of the aorta, from the fifth to the third dorsal vertebrae they are very likely adherent to the aorta, to be actually invading it. At lower levels, though they seemed to be adherent to it, careful and tedious dissection has usually freed them from this organ. This part of the dissection may prove to be very difficult if not impossible from the right thorax. Attempted dissection of a mass which seems to be invading the lung root has seemed more dangerous to us because of the very large venous channels whose position is often not exactly definable until an uncontrollable hemorrhage has occurred. When the mass has been freed from these important structures the resection can continue. There has been occasion when operating from the left to have freed up the esophagus from the diaphragm up to the mass lying at the eighth or ninth dorsal vertebra, only to find the lesion not resectable. One need have little fear evidently for the viability of the esophagus so mobilized as there has been no subsequent perforation or mediastinal infection follow such procedures in this series. In general, it is better to determine resectability when possible before one has carried out the mobilization of the thoracic esophagus. When the mass has been freed from its contiguous structures and the esophagus carefully mobilized by blunt dissection and tireless hemostasis, the hand is passed down the

mediastinum at the aorta and the stomach delivered into the chest. If adequate mobilization has been effected the stomach passes upward in nearly a straight line above the pylorus. The nodes about the cardia are dissected away from the stomach and left on the spleen. The stomach is then cut across just below the cardioesophageal junction and turned in with three rows of sutures. The lower esophagus and mass are turned upward and the stomach is sutured to the esophagus behind the projected level.

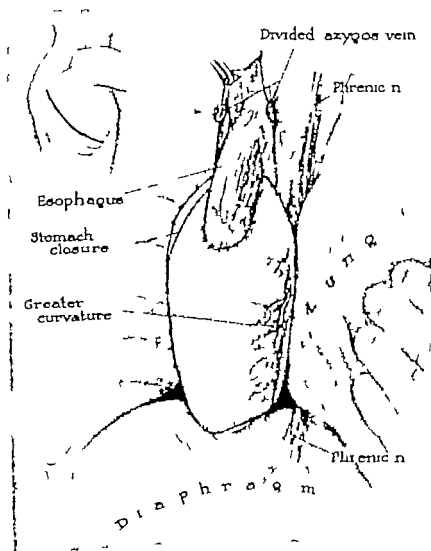


Fig. 3.—Second stage (thoracic approach). The relationship between the transverse stomach, the azygos vein, and the proximal esophagus as they lie in the right chest at the conclusion of the second stage.

of anastomosis. When one row of interrupted silk sutures has been tied the esophagus is transected using a clamp on the distal side only and the specimen is removed. It is believed that the esophagus should not be transected closer than two inches and preferably three inches proximal to the gross lesion. Others have noted the predilection for wide submucosal spread of this lesion. This is one outstanding advantage of the resection when done through the right side of the thorax. The level of the transection may be freely selected without substantially increasing the risk of the operative procedure. This is not usually the case when operating through the left side of the thorax. The retained esophagus should be handled as little as possible during these procedures. Interrupted silk is used in two rows for the anastomosis according to the technique of Sweet. The stomach is then sutured both to the diaphragm at the new hiatus and to the pleura to relieve strain on the anastomotic sutures. The pack is withdrawn and the lung reinflated. The thorax is closed with continuous chromic catgut sutures in the pleurointercostal space and with interrupted fine chromic sutures in the muscular layers. An intercostal drainage tube is used for forty-eight hours. At the conclusion of the skin closure the air is aspirated from the chest through this tube and 50,000 units of penicillin are instilled.

Case 1 (X-60181) — A 34-year-old man, 11 years ago admitted to the Institut complaining of progressive difficulty in swallowing and progressive weight loss. Eighteen months prior to the above period in the same period. Histogenologic examination revealed an ulcerating lesion of the esophagus 4 cm long, 1 cm at the junction of the middle and lower thirds of the esophagus with proximal dilatation of the esophagus and an old healed diaphragmatic ulcer. Esophagoscopy on June 2, 1941 revealed a ulcerating ulcerative lesion 15 cm from the gum line. Biopsy showed some necrotic tissue along with chronic inflammatory tissue. No diagnosis of carcinoma possible on the sections. On July 1, after proper preparation, anal and left iliofemoral and right thoracic resection of the lower third of the esophagus and the upper portion of the stomach carried out. The intrathoracic esophagogastrostomy (anastomosis) successful. The patient discharged from the hospital on July 23. Pathologic study showed an ulcerating lesion with firm induration extending through the entire wall of the esophagus producing almost complete obstruction. The sections however disclosed a non-inflammatory tissue with considerable scarring but no evidence of malignancy. The five biopsies showed ulcer of the lower esophagus with stenosis. A gastric ulcer was recognized in the specimen.

Comment — At operation this lesion, except for a slight rubbery consistency to palpation appeared grossly similar to other lesions in this same location which proved malignant. The changes in the esophageal wall were not due to edema but were the result of long-standing chronic inflammation and presumably were largely permanent.

Case 2 (X-34863) — A 60-year-old man, 14 years ago admitted to the Institut complaining of difficulty in swallowing and progressive weight loss (ten pounds) in four months duration. X-ray studies disclosed ulcerating lesions of the esophagus 10 cm in length at the junction of the middle and the lower third of the esophagus.

Esophagoscopy on April 24, 1947 revealed large ulcer lesion 10 cm below the gum line. This lesion on biopsy proved to be a focal carcinoma. He died on June 10. Despite evidence of impaired renal function as revealed by the phenolphthalein test and Morison's concentration test, the operation was performed. On June 11, combined left thoracic and right thoracic resection.

Comment — The first stage of the procedure was

completed, but after opening the thorax and mobilizing the distal esophagus the man could not be freed from the left lung root. The stomach and lower esophagus were brought up into the right thorax easily through the widened hiatus. These vessels were returned to the abdominal cavity and the hiatus was repaired. The man developed increasing renal uremia on the third postoperative day and died. Uremia was evident after exploration. At autopsy the cause of death was ascribed to advanced chronic interstitial nephritis. In uremic ulcerations of the sigmoid and rectum. The stomach and lower esophagus gave no loss of being viable at the time of death despite the extensive mobilization of these organs during the first stage of the procedure.

#### ADDENDUM

Since acceptance of this paper for publication five additional operations have been done by this method.

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## INTRAVENOUS CHOLECYSTOGRAPHY WITH TETRAIODOPHTHALMIC FLUORESCIN

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SINCE Graham and his co-workers first reported the use of tetrabromophenolphthalein and tetraiodophenolphthalein for cholecystography the latter dye has remained the most commonly used intravenous dye for this purpose. Its popularity as an oral contrast media for gall bladder examination, however, has been largely replaced by Piodax (beta (3,5-diiodo-4-hydroxyphenyl)-alpha phenyl propionic acid).

Many investigators have reported favorably the results obtained with Piodax (oral) as compared with those obtained with tetraiodophenolphthalein given either by the oral or intravenous route. These reports have stressed the reduction in number and severity of toxic symptoms encountered when using Piodax.

The advantages of intravenous cholecystography are very real in some cases. Although a quantity of dye is injected directly into the blood stream, the variable factor of intestinal absorption is circumvented, and the interval before the gall bladder can be visualized is shortened. For this reason it was thought that a report of an additional dye for intravenous cholecystography would be of interest.

Sodium tetraiodophthalic fluorescein was first employed at this clinic in an attempt to increase the radiopacity of certain intracranial lesions. Since it was known that sodium fluorescein itself was largely excreted in the bile, medicinal attempts were made to obtain cholecystogram. Thus, several of the first patients received much more dye than would be necessary for gall bladder visualization alone.

Iodinated fluorescein can be prepared in several ways. Iodine may be substituted directly on fluorescein in which case the iodine is attached to the resorcinol part of the molecule. Erythrosin or tetraiodoresorcinol-fluorescein is an example of the resulting compounds. However, the parenteral use of erythrosin for producing radiopaque shadows is limited by its lack of solubility and its toxicity. In addition its deep cherry red color is objectionable as the patient's skin would be deeply stained.

Of the other than fluorescein compounds in which the iodine is substituted on the phthalic ring possess many clinical advantages. Their solubility is great even with few iodine atoms introduced. The solubility of erythrosin is only

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completed but after opening the thorax and mobilizing the distal esophagus the mass could not be freed from the left lung root. The stomach and lower esophagus were brought up into the right thorax easily through the widened hiatus. These viscera were returned to the abdominal cavity and the hiatus was repaired. The animal developed increasing renal uremia secondary on the third postoperative day and died in uremia seven days after exploration. At autopsy the cause of death was ascribed to advanced chronic interstitial nephritis with uremic ulcerations of the sigmoid and rectum. The stomach and lower esophagus gave evidence of being viable at the time of death despite the extreme mobilization of these organs during the first stage of the procedure.

#### ADDENDUM

Since acceptance of this paper for publication, five additional experiments have been done by this method.

#### REFERENCES

1. Sweet, R. Carcinoma of the Mid Thoracic Esophagus, Ann Surg 121: 637, 1946.
2. Garlock, John. Combined Abdomino-Thoracic Approach for Carcinoma of Cardia and Lower Esophagus, Surg Gynec & Obst. 83: 737, 1946.
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## TOXICITY

Originally tetraiodophthalic fluorescein prepared by us frequently caused nausea and severe intestinal contractions, but later use of more purified samples of the dye resulted in transient nausea in only two patients. There were no instances of vomiting nor did the patients complain of diarrhea which not infrequently follows the use of tetraiodophenolphthalein.

Three patients who received large amounts (9 to 10 Gm.) of tetraiodophthalic fluorescein over a prolonged period developed acute thrombophlebitis of the veins proximal to the site of insertion. This complication, which was not encountered subsequently was probably due to the long exposure of the intima to the alkaline dye solution (pH 10.0).

In two instances appreciable amounts of dye (estimated 30 cc of a 5 per cent solution) infiltrated into the subcutaneous tissue. Although local pain and some redness developed at the site of the infiltration, the transient inflammation regressed rapidly without therapy.

It was noted that all patients were tinted a light flesh-pink color by the dye and this color remained visible in the skin for several hours.

## RESULTS

Twenty-two patients were examined by this method, some with biliary or gastric symptoms and some without (Table I). Two patients had pyloric obstruction, and intravenous cholecystography was necessary to visualize the gall bladder which previously could not be visualized after oral administration of Priodax. The results were (1) good visualization of the gall bladder in the majority of patients (Figs 1 to 4) (2) nonvisualization of the gall bladder

TABLE I. I. INTRAVENOUS TETRAIODOPHTHALIC FLUORESCIN

SUBJECT	DOSE (GM.)	TIME	
		VISUALIZATION	DIAGNOSIS
A. W.	10	3 hr.	Chronic cholecystitis
I. K.	10	4 1/2 hr.	Chronic cholecystitis
E. K.	9	10 h.	Normal
R. H.	8	N. shadow	Acute gall bladder
M. H.	7	8 hr.	Normal
O. J.	6	15 min., 12 hr.	Normal
J. H.	6	4 t. 6 hr.	Normal
E. S.	5	8 hr.	Normal
H. P.	5	4 hr.	Normal
J. H.	5	15 min.	Normal
A. T.	4	N. shadow	Chronic cholecystitis and cholelithiasis
M. T.	3	1/2 to 3 1/2 hr.	Normal
F. L.	3	1 1/2 hr.	Chronic cholecystitis
C. R.		1 hr.	Normal
M. A.		N. shadow	Chronic cholecystitis
D. P.		1 1/2 h.	Chronic cholecystitis
J. F.		N. shadow	Chronic cholecystitis
F. L.	2	3 t. 4 hr.	Chronic cholecystitis
C. R.		N. shadow	Chronic cholecystitis
E. S.	10	hr.	Chronic cholelithiasis

\*Skull studies cholecystography incidental

Supplied in part by Dr. D. L. Tisher, Abbott Laboratories, North Chicago, Ill.



about 10 per cent in water while tetrasodium phthalic fluorescein is approximately 30 per cent soluble. Also, the iodophthalic compounds retain their fluorescence and, in addition, are lighter in color. Thus, they are less apt to cause an objectional staining of the skin.

The toxicity of erythrosin is much greater than that of tetrasodium phthalic fluorescein. Preliminary toxicity studies indicate that the MLD/50 mice getting erythrosin is about 0.5 Gm. per kilogram, while that of tetrasodium phthalic fluorescein is 0.45 Gm. per kilogram.

The pH of the disodium salt of tetrasodium phthalic fluorescein is about 10. Although the monosodium salt has a more favorable pH, a rearrangement to form the disodium salt takes place with the application of heat and the remaining dye precipitates. Further addition of alkali is necessary to get all of the dye into the solution. The resulting solution of the disodium salt of tetraiodophthalic fluorescein is very stable and can be autoclaved. The final product contains 57.7 per cent iodine as compared with 55.2 per cent iodine in sodium tetratiodophenylphthalate.

Hexaiodofluorescein and octaiodofluorescein have been prepared, but their deep color, low solubility and toxicity negate their usefulness.

#### TECHNIQUE

In those instances, at the beginning of the study where the amount of dye given intravenously was over 1 Gm., the dye was added to 5 per cent glucose solution and administered by Murphy drip adjusted to flow the solution to run in over a half-hour period. Roentgenograms of the gall bladder were usually taken four to six hours after completion of the injection.

The final method worked out for gall bladder visualization consisted of the rapid intravenous injection of approximately 40 mg. of dye per kilogram of body weight so that the total dose given adults ranged from 1 to 3 Gm. The dye solution was adjusted so that a convenient volume (15 cc.) contained an individual dose. Direct intravenous injection was made within a period of one to two minutes.

Preparations were negligible. A light fast breakfast was given on the morning of the examination and other preparations were made. The first x-ray view was usually obtained two hours after the injection. If this showed

no visualization, a second view was made in three hours. Only the best upright views were obtained if necessary.

Selection of a two- to three-hour interval for gall bladder visualization was based upon studies made in which radioactive iodine was substituted in a similar dye and counts were made over the gall bladder with a Geiger counter. A marked increase in the counts over the gall bladder region was noted beginning forty-five minutes after injection.

in four cases, and (3) nonvisualization of the common duct in a patient whose gall bladder had been removed previously. In the other four instances the gall bladder was assumed to be pathologic; this was correlated with clinical findings and was verified in two cases by subsequent surgery.

Further studies of tetraiodophthalic fluorescein and related dyes are in progress. It is hoped that the present technique can be varied so as to enable demonstration of the common duct itself. The possibility of administering the dye orally and subsequently studying several organ systems, is under consideration.

In addition, radioactive iodine has been substituted into iodinated fluorescein in order to measure more accurately the blood levels, concentration of the dye in the gall bladder and rates and routes of excretion.

#### SUMMARY

*Intra enous cholecystography utilizing tetraiodofluorescein: a simple rapid and nontoxic method.* Dosage: approximately 40 mg per kilogram. The optimum time for visualization appears to be two to three hours after injection. Subjective evaluation of the gall bladder shadows produced on the films shows densities comparable to those of tetraiod phenolphthalein. A minimum of preparation is necessary to obtain good cholecystograms.

The authors wish to express their appreciation to Dr. W. D. Armstrong, Department of Physiological Chemistry, for use of the facilities of his laboratory and to both him and Dr. Gerald Boyck, Department of Chemistry, for much helpful advice.

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Fig. 1—Intra ocular injection of 0.5 cc. of 1% solution of strychnine hydrochloride in 1% solution of tetracaine hydrochloride. The eye was obtained ten hours after demonstration of strychnine hydrochloride in the eye.



Fig. 2—Chloroform was made four hours after the intra ocular injection of 0.5 cc. of tetracaine hydrochloride in 1% solution of strychnine hydrochloride.



Fig. 3—Rapid intra ocular injection of 0.5 cc. of 1% solution of strychnine hydrochloride in 1% solution of tetracaine hydrochloride. The eye was obtained ten hours after demonstration of strychnine hydrochloride in the eye.



Fig. 4—Same case as Fig. 3. Roentgenogram obtained forty-five minutes later subsequent to fatty acid.

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Intravenous cholecystography utilizing tetraiodofluorescein: a simple, rapid, and nontoxic method. Dosage is approximately 40 mg per kilogram. The optimum time for visualization appears to be two to three hours after injection. Subjective evaluation of the gall bladder shadows produced on the films shows densities comparable to those of tetraiodophenolphthalein. A minimum of preparation is necessary to obtain good cholecystograms.

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FIG. 1.—Intra esophageal injection of .5 gm of tetraiodophthalic barium sulfate. Incidental x-ray was obtained ten hours to demonstrate gall bladder filling.

FIG. 2.—Cholecystogram made four hours after the intra esophageal injection of .5 gm of tetraiodophthalic barium sulfate.



FIG. 3.—Rapid intravenous injection of 100 cc of 40% contrast medium. Roentgenogram made after four hours to demonstrate nonobstructive calculus.

FIG. 4.—Same case as Fig. 3. Roentgenogram obtained forty-eight minutes later, subsequent to fatty meal.



tubes of polyethylene have been implanted permanently. Experimental studies have also suggested that polyethylene film be used in place of rubber for many temporary appliances, namely for Penrose and rubber tissue drains, and to prevent adhesion of certain structures between stages of multiple stage operations.

As evidence accumulated in this laboratory that polyethylene was a superior material for implantation in tissue a method of molding polyethylene into special forms became the object of a particular search. The immediate concern in this search was to make a tube for anastomosis of parts of the common bile duct the hypothesis being that because polyethylene (like its simpler form, ordinary paraffin) is not wetted by aqueous solutions, bile solid would not precipitate on the wall and occlude a tube of this material. It was soon recognized that commercially extruded tubing had a very limited use and that such tubing was not a suitable material out of which to mold objects. Commercial tubing is relatively thick walled at molding temperatures the tubing contracts longitudinally wall thickness increases, and the internal diameter decreases. When such tubing is drawn while it is at molding temperature both thickness of the wall and internal diameter decrease. It was discovered also that it was impossible to weld flanges or ridges to commercial tubing without serious local encroachment of the lumen.

Eventually a method of making tubes and several other appliances out of polyethylene film was evolved. During the evolution of this method many peculiar properties of polyethylene came to be recognized.

#### ✓ PROPERTIES OF POLYETHYLENE

Polyethylene tubing or thick film is semitransparent and has a pearly gray color. It is tasteless has a slippery feel and a very low coefficient of friction. It conducts heat very poorly and is an excellent electric insulator. Specific gravity is 0.9. Thin film of less than 0.001 inch (0.025 mm.) is transparent and colorless. Polyethylene softens and is therefore moldable at temperatures above 110° C. As polyethylene softens it contracts in all planes, like glass. The degree to which contraction occurs varies with thickness, as indicated later. Between 60° and 110° C. polyethylene is slightly more pliable and soft than at lower temperatures, and molded or extruded objects tend to become distorted slightly in boiling water. It is less hard than lucite but harder and much tougher than ordinary paraffin. Flexibility varies with thickness, thin film or thin walled tubing being extremely flexible. Polyethylene does not crack or break and it can be cut easily with knife or saw. It is elastic to bending and somewhat elastic to stretching force. The material, having a high tensile strength, can be drawn out considerably before it tears. It holds a suture very well. One of the most significant qualities of polyethylene is that its surface is not wetted by water or aqueous solutions.

Chemically polyethylene is quite inert. It is unaffected by strong or weak acid or alkalis or powerful reagents such as fluorine gas. At temperatures of 60° C. or less it is unaffected by all known solvent. Pure polyethylene produces no tissue reaction, either inflammatory or foreign body.

# METHOD OF MAKING TUBES OF POLYETHYLENE FILM FOR USE IN ANASTOMOSIS OF THE COMMON BILE DUCT TRACHEA, AND PELVIC COLON

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THROUGHOUT the history of surgery a material has been sought which, although a foreign substance could be used for surgical reconstruction of various organs and which would neither undergo change itself nor produce remote or local changes within the body. Of the many materials that have been tried few have enjoyed continued popularity and use. Organic substances, such as animal membrane and rubber produce more or less reaction and ultimately are resorbed or become deteriorated. Certain metals and alloys, notably tantalum and titanium, have been useful for some purposes. The usefulness of tantalum and titanium is limited however because of certain physical characteristics, for example their opacity to roentgen rays and their tendency to become overheated during application of short wave therapy to surrounding tissue and because of rigidity and hardness. In the case of titanium and of high cost in the case of tantalum. Lucite known also as plexiglas has proved to be a most satisfactory plastic material for many purposes. The disadvantages of lucite are that it is not flexible and that thin walled articles are both difficult to make and brittle.

A variety of other plastic materials have been investigated recently. The polyvinyl resin series of plastics have common disadvantage. They contain more or less of certain organic solvents, known as plasticizers, in order to make the plastic more flexible and translucent. Unfortunately the plasticizers are slowly leached out of the plastic by many organic solvents, including those present in body fluids. Not only as plasticizers more or less irritating to tissue but the plastic becomes opaque, hard, and rather brittle.

Another plastic which has received attention recently is polyethylene, or polythene. Polyethylene is formed in polymerization of ethylene and might be described as being ordinary paraffin which has been polymerized to a greater degree. Polyethylene is manufactured by a patented process and is then furnished to various manufacturers who convert the raw material to commercial products by an extrusion process. The extruded product is, as far as known, either tubing, flat film, or rods.

Polyethylene is a material which some of us have found superior to metallic or other plastic materials for surgical implantation in living tissue. A few experimental studies have been carried out in this laboratory and others are in progress, which encourage us to believe that commercial polyethylene film and tubing will be useful in clinical surgery. Film has been permanently implanted to replace areas of dura or nasal membrane and enterostomy,

tubes of polyethylene have been implanted permanently. Experimental studies have also suggested that polyethylene film be used in place of rubber for many temporary appliances, namely for Penrose and rubber tissue drains, and to prevent adhesion of certain structures between stages of multiple stage operations.

As evidence accumulated in this laboratory that polyethylene was a superior material for implantation in tissue, a method of molding polyethylene into special forms became the object of a particular search. The immediate concern in this search was to make a tube for anastomosis of parts of the common bile duct the hypothesis being that, because polyethylene (like its simpler form, ordinary paraffin) is not wetted by aqueous solutions, bile solids would not precipitate on the wall and occlude a tube of this material. It was soon recognized that commercially extruded tubing had a very limited use and that such tubing was not a suitable material out of which to mold objects. Commercial tubing is relatively thick walled at molding temperatures the tubing contracts longitudinally wall thickness increases, and the internal diameter decreases. When such tubing is drawn while it is at molding temperature both thickness of the wall and internal diameter decrease. It was discovered also that it was impossible to well flanges or ridges to commercial tubing without serious local encroachment of the lumen.

Eventually a method of making tubes and several other appliances out of polyethylene film was evolved. During the evolution of this method many peculiar properties of polyethylene came to be recognized.

#### ✓ PROPERTIES OF POLYETHYLENE

Polyethylene tubing or thick film is semitransparent and has a pearly gray color. It is tasteless, has a slippery feel, and a very low coefficient of friction. It conducts heat very poorly, and is an excellent electric insulator. Specific gravity is 0.97. Thin film of less than 0.001 inch (0.127 mm) is transparent and colorless. Polyethylene softens and is therefore moldable at temperatures above 110° C. As polyethylene softens it contracts in all planes, like glass. The degree to which contraction occurs varies with thickness, as indicated later. Between 60 and 110° C. polyethylene is slightly more pliable and soft than at lower temperatures, and molded or extruded objects tend to become distorted slightly in boiling water. It is less hard than lucite but harder and much tougher than ordinary paraffin. Flexibility varies with thickness, thin film or thin walled tubing being extremely flexible. Polyethylene does not crack or break and it can be cut easily with knife or scissors. It is elastic to bending and somewhat elastic to stretching force. The material has such a high tensile strength can be drawn out considerably before it tears. It holds a suture very well. One of the most significant qualities of polyethylene is that its surface is not wetted by water or aqueous solution.

Chemically polyethylene is quite inert. It is unaffected by strong or weak acids or alkalis or powerful reagents such as fluorine gas. At temperatures of 60° C. or less it is unaffected by all known solvents. Pure polyethylene produces no tissue reaction, either inflammatory or foreign body.



## ✓ TECHNIQUE OF MOLDING POLYETHYLENE TUBES

The underlying principle of this technique of making tubes is the fact that when polyethylene is heated to the point where it becomes soft, it shrinks. To take advantage of this characteristic, a sheet of thin film is wrapped around a form which is a metal tube. When the film is heated and becomes soft it not only fuses layer to layer but the whole thickness of the wall shrinks tightly and uniformly to the metal tube or form. In other words, the molding pressure or force is the shrinking force of the polyethylene itself. Such a method automatically creates a problem that of removal of the polyethylene tube after it has fused and has shrunk tightly to the form. Obviously the form must be coated with a lubricant that will not be affected by heat and the lubricant must also be covered by some material which will prevent incorporation of lubricant in the polyethylene during fusion. The latter material must be easily removable from the finished polyethylene tube.

The several steps in the technique are accordingly the coating of the form with a lubricant (soap), the covering of the lubricant with a material that can be removed from the finished tube (cellophane), the wrapping of the form with polyethylene film, the fusing of the film with heat, and the removal of the finished tube from the form.

The metal tube to be used as a form should have a uniform diameter and it should be perfectly round free from dents and ridges, and smoothly polished. Its external diameter must be the same as the inside diameter of the polyethylene tube that is to be made. In other words, when one wishes to make a tube with a certain inside diameter of form having an outside diameter of that measurement is selected.

Thin walled brass tubes seem to make the best forms. This is probably because brass, which is a good conductor of heat prevents overheating and burning of the polyethylene when too much heat is applied to one portion of the tube. A tube rather than a rod is used because the latter heats too slowly and because it is difficult to remove a polyethylene tube from a rod. Ordinarily it is best that the brass tubes be about 1 foot (30 cm) long. Shorter tubes may be used if a handle is attached.

## Steps in Making Polyethylene Tubes

1. Coating of brass tube. A film of thick solution of a good grade hand soap is applied evenly to the brass tube and allowed to dry. All that portion of the tube about which film will later be wrapped must be covered in soap solution but it is well not to get soap on the rest of the tube. If there is soap on the non-wrapping portion of the tube the technician may get it on his fingers and then use on the polyethylene film. Soap on the film will pull the tube when it is fused.

Cellophane wrapping. Next a sheet of cellophane is wrapped tightly about the brass tube over the non-wrapping part by the soap film. The cellophane should be as wide as the length of tube or rod by soap film at least 2 in. wider than the length of polyethylene tube to be accomplished making. Only enough cellophane to make two thicknesses is used. A satisfactory cellophane for this use is nonwovens of P. T. 300 (Du Pont). It is reported that the film have no creases or wrinkles and that the edge be not curled.

3 *Polyethylene wrapping* To make the wall of the tube while the cellophane film is prevented from unrolling by holding it firmly between the thumb and finger tips, wrapping of the polyethylene film is started. The latter film will form the wall of the finished tube. The width of this film must be the same as the length of the tube to be made. In other words, to make a tube 1 cm long one uses a strip of film 5 cm wide.

The thickness of the film used is most important. Film thicker than 0.004 inch (0.102 mm) cannot be used because during the process of heat fusing, it wrinkles longitudinally, thus making a short and thick walled tube. Film having a thickness of 0.003 to 0.004 inch (0.076 to 0.102 mm) is best for tubes which are to have an internal diameter of 4 mm or more. Because it is more easily rolled 0.002 inch (0.051 mm) film is preferred for tubes with an internal diameter of less than 4 mm. The number of turns of film wound in this tube determines the thickness of the wall of the tube. Five turns, or film thicknesses of film, produce a tube with a thick but sufficiently rigid wall for most purposes.

After the desired number of turns of film have been wrapped and the unused strip of film has been cut off, the film is tightened by holding the handle of the brass tube in one hand and gripping the polyethylene-covered portion of the glass tube in the other hand. The two hands are then rotated in opposite directions, thus tightening the film. If the film is not tightly wrapped there will be air spaces between layers of film and when the tube is heated the air spaces will become bubbles. After the film has been tightened it is held in place by a tightly wound rubber band.

Thin ridge wide bands, or flanges may be placed on the outside of the tube at any point. They are made by wrapping narrow strips of film at the point where the ridge band, or flange is desired. Film for these structures is cut into long strips which for the usual tube with an internal diameter of 4 mm or more are from 0.5 to 1 cm wide. The wider the strip the wider the band and the higher the ridge will be. The greater the number of turns or layers, the thicker the ridge or band will be.

A ridge is made by using a strip of film having a thickness of 0.004 inch or more. The best ridges are made with film of a thickness of 0.004 or 0.006 inch (0.102 or 0.152 mm). Bands and flanges are made by use of film of the same thickness as that used to make the wall of the tube.

Winding strips of film on the tube is not difficult. Marks are made with the fingernail on the edge of the film used for the wall of the tube, these marks being made where the ridges or bands are located. One end of the strip is slipped a short distance under the edge of the film of the tube wall and centered under the nail mark, then the wrapping is begun. When enough turns have been made to make the desired thickness of ridge or band, the unused portion of the strip is cut off and the wound strip held in place with a neutral suture. The suture must be placed about the center of the band of film. Designated with N-000 or 0000 is a satisfactory suture. Here cotton thread may be used. The ridges of tubes to be used for temporary splints, for example, the two-piece tube for colon anastomosis after an anterior resection. If a radiopaque marker

is desired (polyethylene itself is nonradioactive) a ligature of silk or tantalum, or other surgical wire suture is used.

4 *Fusing the tube:* The rubber band holding the film of the tube wall is removed. Loosening of the film will not now occur because it is held by the strips and their ligatures. If a band or ridge has not been placed near the end of the tube or if there is a very long distance between ridges or bands, it is well to tie a heavy cotton ligature around the ends of the tube or in the middle of the long interval. Such ties do not become imbedded in the tube wall and may be slipped or cut off the tube after it is fused.

The wrapped tube is fused by heating it to 110 to 115 C. In practice it is far easier to govern the degree of heat by adjusting the distance between the source of heat and tube than by control of the source of heat. It is difficult to watch the fusing process closely in an oven and to remove the tube at the proper instant. Satisfactory sources of heat are an electric hot plate or a Bunsen burner covered by a wire and asbestos screen. If the latter source is used, the burner should be adjusted to give a gentle blue flame.

As the polyethylene-covered portion of the brass tube is held over the source of heat, usually about 1/2 inches (5 cm.) above the hot plate or wire and asbestos screen, it is rotated evenly. Within one minute, longer if the mass of tube is large, the polyethylene begins to become translucent. When it is completely translucent the tube is fused and must not be heated to a higher temperature. If only one end or portion of the tube is completely fused at this point, the brass tube is held tilted so that the finished end is farthest from the source of heat. As soon as all the polyethylene tube is fused it is cooled by passage of cold water through the brass tube.

If the tube has been designed to have bands or flanges and has, therefore, had several turns of thin film wound at the appropriate intervals, the strips remain flat during the fusing process. All that happens is that the several layers of each strip and the tube wall fuse together. A flange is made simply by pinching a band at some point on its circumference while it is still soft with a blunt pointed mosquito forceps.

If strips of thick film (0.005 in. [0.127 mm.] or more) have been used to make ridges, a peculiar change takes place in the strips as they fuse. At first the edges of such strips thicken and ripple and, simultaneously, the two edges draw close to the ligature which is midway between the edges. The edges continue to thicken and curl outward. A moment later the edges on each side of the ligature have met over the ligature and have fused evenly together. Fusion of the ridge is complete when these changes have occurred in all layers of the strip and the mass is homogeneous and translucent. The finished ridge is broadest at its base where it is fused to the wall of the tube and has a feature buried in the middle of its mass.

5 *Removal of the tube from the form:* Any heavy cotton ligatures which have been placed about the tube to keep the film tightly rolled during the fusing process are removed. Cellophane which protrudes beyond the ends of the fused tube is removed by pressing a knife against the edge of the tube while the

brass tube is rotated. Next the handle or free end of the brass tube is gripped firmly with one hand and the polyethylene tube with the other. Rubber gloves, or a piece of rubber dam held in each hand, prevent slipping and are a great help in this manipulation. As the hands are forcefully rotated in opposite directions the polyethylene tube along with its lining layer of cellophane becomes loose and can be slipped off the brass tube easily. The soap film both prevents cellophane from sticking to the brass form and lubricates the inner surface of the cellophane.

The lining layer of cellophane may be freed from the tube easily by running a blunt pointed thin instrument between tube and cellophane. After it is freed the cellophane layer may be collapsed and extracted.

#### EXAMPLES OF MOLDED POLYETHYLENE TUBES AND APPLIANCES

A variety of molded polyethylene tubes have been made for experimental studies which are in progress in this laboratory. The following tubes are examples (Fig. 1).

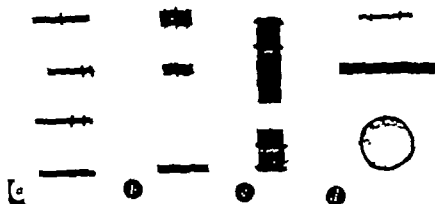


FIG. 1—Examples of various types of molded polyethylene tubes and appliances. (a) Tubes for use in the common bile duct. Four different types of tubes for use in common duct anastomosis are shown. (b) Tubes for use in the T tube. The top tube is the type used for end-to-end anastomosis of parts of the tract after resection of a portion of the tract. The bottom tube is used for irrigation of the tract or main biliary. (c) Tube for use in common bile duct. The tube is placed in the duct and secured with a suture. (d) Other tubes and appliances. A thick tube of large diameter.

#### Tubes for Use in the Common Bile Duct—

*End-to-end anastomosis.* A few tubes of this type have been used clinically. These are thin-walled tubes, their wall having a thickness of 0.004 inch (0.102 mm) film with an internal diameter of 4 mm. The tube is highly flexible which facilitates its insertion into the two limbs of the duct. It contains a feature is a centrally placed ridge one side of which has been flattened by pressure on the ridge while it was in the soft state. The other side of the ridge constitutes a tab which will protrude through the duct wall at the

the of repair. A silk suture is passed with an ordinary surgical needle through the substance of the tab and anchored to the wall of the duct on either side of the tab. These tubes may be made in any length and may be cut to the desired size with scalpel or scissors at the time of operation.

*For a lumen of the common bile duct and the side of the jejunum or duodenum.* This tube resembles the tube for end-to-end anastomosis of part of the common duct except that it has no central ridge. Instead it has a ridge at one end and another slight larger ridge about 8 mm behind the distal ridge. This collar-button-shaped end of the tube is inserted into a small hole in the side of the duodenum (or a loop of the upper part of the jejunum). The tube is placed so that the bowel wall is between the two ridges. An interrupting purse-string suture closes the bowel about the tube. The free end of the tube, after the tube has been cut to the desired length, is inserted into the common duct. Interrupted silk sutures approximate the edge of the common duct to the duodenal or jejunal wall adjacent to the purse-string suture. One or two of these interrupted silk sutures include the outer ridge of the tube.

*For anastomosis of the common duct and the side of a Y loop of jejunum.* A variation of the tube last described has been constructed for use in a modification of the operation described by Allen, an operation in which anastomosis of the remnant of the common duct and the end of a Roux Y loop of jejunum is established. In this operation the end of the jejunum is first entered a short distance. Because at least 1 cm of the jejunal wall has to be turned in, the two ridges of the collar-button shaped end of the tube are placed about 1.6 cm apart. Also the end of the tube is allowed to project about 5 mm beyond the terminal ridge. When the tube is in place the terminal ridge and projecting tip of the tube should be inside the end of the blind loop and the other ridge should be close against the outer folded edge of the end of the Y loop. The free end of the tube lies in the common duct, and the edge of the common duct remnant is sutured to the edge of the bowel in the previously described operation.

#### *Tubes for Use with Traube and Brock —*

*For end-to-end anastomosis of the main portion of the track.* Such tubes have a diameter comparable to that of the track. At each end of the tube there is a ridge and in the middle there is a band with small flange. In the anastomosis of part of the track as in this tube it is necessary to have the ridge at each end placed between traheal rings. One of the interrupted silk sutures must transfix the flange in the center of the tube.

*For implanting the track into the bronchus.* These tubes differ from the one just described only in that they have flanges rather than ridges at each end; the flanges serve to strengthen the tube where it will have the greatest tendency to collapse or become indurated. During the closure of the longitudinal incision in the posterior tracheal or bronchial membrane through which the tube is inserted, one of the interrupted silk sutures should transfix the flange.

All the head or bronchial tubes should be about twice as long as their diameters.

*Temporary Tube for Use in Anastomosis of the Colon and Rectum After Excision of the Distal Part of the Colon*—This device is a two-piece tube, one piece of which fits inside of the other making a snug sleeve union. Each piece of this tube has two ridges, one of which is at one end of the piece and the other 2 cm from the end. The outside piece is short being only about 3.5 or 4 cm long. The inside piece is about 1 cm long. After the colon has been inserted and the crushing clamps removed from the rectum and proximal part of the colon, the inside piece of the tube is inserted into the end of the proximal part of the colon and the outside piece into the rectum through its open end. The ridge ends of both pieces being placed inside the bowel. The gut purse-string sutures, which have been previously placed at the crushed edge of each portion of the bowel, are then tied and the inside or proximal tube is inserted into the distal tube. The ends of the purse-string sutures are tied together. An outer layer of interrupted silk sutures which are easy to place because the tube within the bowel acts as a splint completes the anastomosis.

After about one week, more or less, depending on the size of catgut used for the purse-string sutures, the tube is passed rectally spontaneously. In the meantime all bowel content enters the tube proximal to the site of anastomosis and is conducted past the anastomosis through the inside tube. The double ridges of the tube on each side of the anastomosis protect against the passage of fecal content along the outside of the tube.

*Other Special Tube and Appliance*—It is possible to make tubes with small diameters and thin walls, with ridges or flanges, for use in blood vessels, brain ventricles, nasal sinuses, and so forth. The film which is 0.001 inch (0.01 mm) thick is best for such tubes, the number of thicknesses depending on the desired thickness of the wall of the tube.

Tubes with walls of one layer thick can be made although one side of the tube will be two layers thick where the film is overlapped. A couple of layers of cellophane are wound tightly over as well as under the film in this case. After the fusion operation the outside layer of cellophane must be peeled off carefully before the tube can be removed from the form.

As a variation of the technique described herein one can apply a polished bone handle or ridge to the edge of a bag of thin film. The handle or ridge is wound about the edge of the bag near the end of a form, and the bag portion is covered by a metal cap. The metal cap is kept cool during the fusing process by covering it with a wet towel. If the metal cap were not kept cool the bag beneath it would become soft and then would shrink and thicken.

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of a pair. A silk suture is passed with an ordinary surgical needle through the substance of the tab and anchored to the wall of the duct on either side of the tab. These tubes may be made in an length and may be cut to the desired size with scalpel or scissors at the time of operation.

*For anastomosis of the common bile duct and the side of the jejunum or duodenum.* This tube resembles the tube for end-to-end anastomosis of part of the common duct except that it has no central ridge. Instead, it has a ridge at one end and another slightly larger ridge about 8 mm. behind the distal ridge. The collar button-shaped end of the tube is inserted into a small hole in the side of the duodenum (or a loop of the upper part of the jejunum). The tube is placed so that the bowel wall is between the two ridges. An inverting purse-string suture closes the bowel about the tube. The other end of the tube, after the tube has been cut to the desired length, is inserted into the common bile duct. Interrupted silk sutures approximate the edge of the common duct to the duodenal or jejunal wall adjacent to the purse-string suture. One or two of these interrupted silk sutures include the outside ridge of the tube.

*For anastomosis of the common duct and the end of a loop of jejunum.* A variation of the tube last described has been constructed for use as a modification of the operation described by Allen, an operation in which anastomosis of the remnant of the common duct and the end of a Roux-Y loop of jejunum is established. In this operation the end of the jejunum is first inserted at a short distance. Because at least 1 cm. of the jejunal wall has to be turned in, the two ridges of the collar button-shaped end of this tube are placed about 15 cm. apart. Also the end of the tube is allowed to project about 5 mm. beyond the terminal ridge. When the tube is in place the terminal ridge and projecting tip of tube should be inside the end of the blind loop and the other ridge should be close against the outside folded edge of the end of the Y loop. The free end of the tube lies in the common duct and the edge of the common duct remnant sutured to the edge of the bowel as in the previously described operation.

#### *Tubes for Use in the Trachea and Bronchi —*

*For end-to-end anastomosis of the side of the portion of the trachea.* Such tubes have a diameter comparable to that of the trachea. At each end of the tube there is a ridge and the middle there has a small flange. In the anastomosis of part of the trachea or a fistula it is necessary to place the ridge at each end placed between tracheal rings. One of the interrupted silk sutures must transfix the flange in the center of the tube.

*For anastomosis of the trachea and bronchus.* These tubes differ from the one just described only in that they have bands instead of ridges. At each end, the bands serve to strengthen the tube where it would be the greatest tendency to collapse become distorted. During the closure of the longitudinal incision in the trachea or bronchus or bronchial membrane through which the tube is inserted, one of the interrupted silk sutures should transfix the flange.

distention and palpable bowel loops coexist in a patient who has frequency and urgency of stool. The picture is further clouded by variation of daily symptoms. One day the edema and inflammation in the region of the fistulous communication may be so severe as to cause partial to complete obstruction of both the involved sigmoid and the ileum. Then the edema obstructing the ileum may subside and frequent stools occur because of ileal contents emptying into the sigmoid and at the same time cramping pains and signs of partial colon obstruction may exist because of edema and induration blocking the sigmoid. Again the edema may block off the fistula and the ileal contents take their normal course to the colon only to meet obstruction in the sigmoid, in which event the clinical picture of sigmoid obstruction is again present. In these cases, the diagnosis of complicated ulcerative colitis, amebic or bacillary dysentery or carcinoma of the sigmoid and rectum must be considered.

With obstruction threatening barium should not be given by mouth. Also, one hesitates to give a barium enema but probably no harm will result if the radiologist is informed that an acute inflammatory condition possibly exists in the sigmoid and is impressed with the necessity of giving the barium enema very slowly and carefully and under low pressure. The barium enema may reveal a sigmoidal obstruction and some diffuse spread of the barium which is difficult to interpret. If not contraindicated by severe peritoneal reaction and abdominal tenderness, a proctoscopic examination will aid in eliminating the presence of low sigmoidal carcinoma or ulcerative colitis. At times, it is necessary to postpone proctoscopic examination for some days, but in any event it should be done before malignancy or ulcerative colitis is excluded. If the barium enema reveals a diverticulum one may have a lead to the probable course of event and establish a diagnosis. However because of the acuteness of symptoms, with fever, leucocytes, and localized tenderness, one rightly tends to postpone a barium enema study and thus diagnosis is delayed. If no diverticulum is visible on the roentgenograms and there has been no previous diagnosis of diverticular disease of a perforating lesion with fistulous communication between the sigmoid and ileum is most difficult unless it is established that barium has entered the small intestine directly from the sigmoid. However by correlating the events in the history just described with the abdominal examination, x-ray findings, and exclusion of rectal pathology by proctoscopic examination the diagnosis can usually be made.

In the four cases presented here two patients had associated pain in the upper abdomen and the diagnosis of gall bladder disease had been made elsewhere. In one a cholecystectomy had been done and the patient stated that the surgeon had described a "strawberry like gall bladder" to her. It is true that inflammation of pelvic organs or the pelvic colon may give rise to a peritonitis in the region of the liver and diaphragm, and one must be alert to this syndrome.

The syndrome of partial obstruction and urgency and frequency of stool occurs not too infrequently and many times leads to the incorrect diagnosis of inoperable rectal or sigmoidal carcinoma. Spontaneous recovery may occur after such a diagnosis with credit directed to either the ingested medicine or a cathartum followed.



# MANAGEMENT OF THE ILEOSIGMOIDAL FISTULA IN DIVERTICULITIS

## CLINICAL SYNDROME AND REPORT OF FOUR CASES

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IN GENERAL, the management of acute diverticulitis should be conservative even though the patient may appear acutely ill and, as not infrequently occurs, a partial to complete sigmoidal obstruction exists. The true or false diverticulum becomes inflamed because of inadequate drainage, probably due to an impaction of the diverticulum which irritates and causes ulceration of the body or neck of the sacculation. As in acute appendicitis, this inflammatory reaction may subside, but, unlike appendicitis, mortality figures reveal that the diverticulum does not so often perforate and cause general peritonitis and death. The inflammatory reaction of the diverticulum results in edema and induration of the sigmoid and of the mesosigmoid which encroaches upon the sigmoid lumen.

The patient with acute diverticulitis generally complains of lower abdominal pain and tenderness situated more to the left or in the midline and not infrequently a mass can be felt. The pain may be cramping. Fever and leukocytosis are usually present. Nausea and vomiting, distention, and intestinal cramping and obstruction vary with the degree of obstruction of the colon and the extent of the inflammatory spread. A scout film may reveal dilated loops of small bowel, but most frequently reveal an enlarged colon and cecum. Low pressure barium enema studies may expose diverticula, narrowing of the involved segment, or complete obstruction. It is remarkable how frequently these patients improve after the gastrointestinal tract is placed at rest by instituting nasogastric or intestinal suction, hot abdominal packs, warm rectal irrigations, and antispasmodics. We are inclined to use penicillin if tender mass is palpable and there is increased fever and leukocytosis.

Usually within two to four days the inflammatory reaction begins to subside and clinical improvement gradually follows. If obstruction has been present gas and intestinal contents begin to build through the narrowed segment of sigmoid. This improvement probably occurs when the neck of the inflamed diverticulum or diverticula opens by natural subsidence of pressure necrosis, and drainage from the sacculations is permitted. When the inflammation does not subside, pressure necrosis may cause the blocked diverticulum to perforate resulting in a localized abscess or generalized peritonitis. When a localized inflammatory mass or abscess develops, loops of distal ileum usually become involved as part of the protective wall. Eventually at times the necrotizing action is sufficient to effect a break in the wall of the ileum with a resultant fistulous communication between the ileum and sigmoid. If the sigmoid has been obstructed and a ileosigmoidal fistula has developed, the clinical picture is rather confusing. Abdominal cramps, active peristalsis, abdominal

eliminated, and there is no history of frequent stools. X-ray studies do not reveal a communication between the sigmoid and ileum at this time.

The third patient insisted on closure of the colostomy. After one year x-ray studies continued to show marked constriction of the sigmoid. At operation, the segment of sigmoid with attached ileal loops was resected. The remaining end of ileum were closed and a primary anastomosis of the sigmoid was accomplished. The colostomy stoma was closed three weeks later.

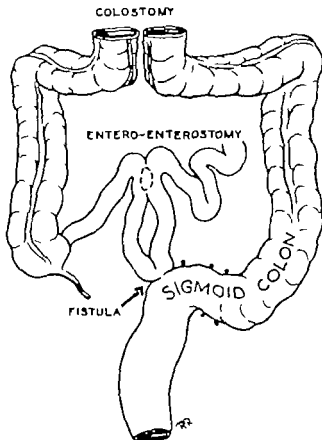


Fig. 1.—Transverse short-circuiting bowel resection around the iliosigmoidal fistula in a man aged 40. The colostomy places the thickened, inflamed sigmoid with narrowed lumen.

The fourth patient, following the short-circuiting procedure and establishment of a colostomy of the transverse colon, gained twenty pounds in weight and refused further surgery including closure of the colostomy. About fourteen months after the operation she again became quite anemic. A small mass was still palpable in the lower abdomen just to the left of the midline. Proctoscopic examination revealed negative findings, but when barium was given only a very small channel was present through the lower sigmoid region. Diver ticula were still visible. Although the patient denied passage of blood per rectum through the colostomy she finally divulged the fact that she had had several episodes of bleeding from the rectum and had passed black

When an inflammatory mass is present and diverticulosis exists, diverticulitis may be suspected. Malignancy may not be definitely excluded and an exploratory operation is recommended. Since the general condition of the patient is usually rather poor the body fluid and chemical imbalance should be corrected and the serum proteins, red blood cells, and hemoglobin brought to a level compatible with undergoing a major surgical procedure. A nonabsorbable sulfonamide sulfathiazole having been on hand of choice lately is prescribed in appropriate dosage. This is roughly calculated at 0.1 Gm. per kilogram weight for the initial dose and the daily maintenance dose is similarly estimated, usually being about  $1\frac{1}{2}$  Gm. four times a day. This is continued for five days or until time of operation. The degree of active infection determines whether penicillin should be given but in any event penicillin is begun the day preceding operation. Nasogastric or nasointestinal suction is employed as indicated and is always instituted the evening before operation. Hot abdominal packs and warm rectal irrigations under low pressure may prove beneficial.

These four cases presented rather similar pictures at operation. A large inflammatory mass occupied the midabdomen at the level of the umbilicus. From palpation and appearance it is difficult to differentiate an inflammatory mass secondary to a perforated diverticulum of the sigmoid and adherent small bowel from a large infiltrating carcinoma of the sigmoid with small bowel involvement and a probable associated abscess. A one-stage procedure is preferable, but this was precluded in these four cases by the severe inflammatory reaction, density of adhesions, degree of edema and the general condition of the patient.

In the presence of a fistula between the ileum and sigmoid, small bowel contents must be diverted from the inflammatory mass and sigmoid, or the symptoms of frequency and urgency of stool will continue. In these cases, a lateral anastomosis was made between the loops of ileum entering and leaving the inflammatory mass, thus permitting small bowel contents to bypass the communicating fistula and inflammatory mass (Fig. 1). Consideration was given to dividing the loops leading to the tumor mass to be sure that ileal contents were completely diverted. This did not seem desirable because if the fistulous communication between the closed loops of ileum and the sigmoid blocked off, blind loop of ileum would have resulted. From the experimental work of Stone, Bernheim, and Whipple, Hartwell and Hogue, and Murphy and Brooks, it was demonstrated thirty years ago that closed loops of ileum 1 ft. within the abdomen resulted in toxic states, chemical imbalance and death as in true obstruction of the small bowel. The sigmoid placed at rest in establishing a colostomy of the transverse colon.

One of these patients does not keep the colostomy of the transverse colon. Usually she has a very slight amount of rectal discharge. A slight bowel movement once each day. She has no discomfort except normal and has gained 12 lbs. (over 8 pounds) weight.

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# TUMORS OF THE SMALL INTESTINE

HOWARD A. WIENBERGER, M.D. AND RUDOLF M. PALTAUF, M.D.  
NEW YORK, N. Y.

(From the Surgical Services and the Division of Laboratories, Lenox Hill Hospital)

## INTRODUCTION

IN CLINICAL investigations and classifications of tumors of the gastrointestinal tract, the emphasis has commonly been placed upon those new growths involving the stomach and the large bowel. This is understandable in view of the fact that the incidence of tumors at the extremities of the gastrointestinal tube is far greater than the incidence of those encountered in the interval small bowel segments. In terms of the known etiologic concepts and postulations on tumor growth it is perhaps not simple to explain the rarity of small bowel neoplastic processes. Certainly the concepts based upon embryologic rests cannot explain the low incidence of small bowel new growths as compared to the number met with in the stomach and large intestine. The various theorems with regard to chronic irritation may perhaps apply in that the small bowel content is generally fluid as contrasted to semisolid and solid constituents of stomach and colon. Assuredly there is a variety of materials secreted by and eliminated into the small intestine which can be classed as chemical irritants. The duodenum for example is constantly bathed in an abundant outflow of gastric juice, bile, pancreatic juice, and mucosal secretions. Still, the incidence of duodenal malignancy is distinctly low.

In spite of the rarity of small bowel tumors, it is imperative that we exhaust all ingenuity in elaborating mechanisms referable to diagnosis and treatment. And this is so because we are confronted with the fact that malignancy of the small bowel is an extremely lethal disease.

## ANALYSIS OF CASES

*Incidence.*—From the point of view of number of cases, our experience with tumors of the small intestine has been limited. After careful study of our files covering the last forty years, we have compiled a report on a total of 20 primary tumors of the small bowel; the clinical record on one of these cases is unavailable. Instances of ampullary tumors of the duodenum are omitted from this study because they are probably largely of duct origin. This number represents approximately 1 for every 3,300 surgical and autopsy specimens studied in this hospital. There are in our files records on 1,410 neoplasms of the gastrointestinal tract, from the esophagus caudad. Thus, small bowel tumors have been encountered at the rate of 1 for every 71 neoplasms elsewhere in the gastrointestinal tract. In spite of this small total number it is interesting to note that 5 of the total of 20 were encountered during the year 1945.

In reviewing the literature on the subject of small bowel tumors, it is evident that our experience is the usual one in that these tumors are conspicuous for their rarity.

fecal material through the colostomy. Because of the anemia the patient was given a blood transfusion and surgery advised. At operation, the large inflammatory mass which was present at the original operation was only a small, hard, craggy mass. Carcinomatous transplants were present on the peritoneum and metastatic nodules were palpable in the liver. No further surgery was attempted. This exemplifies what may be present in an inflammatory mass associated with diverticulitis.

## SUMMARY

A report is made of four cases in which acute diverticulitis of the sigmoid had resulted in the formation of a fistulous communication between the sigmoid and a loop of ileum. The patients were very ill and presented a bizarre set of symptoms, suggesting intermittent bowel obstruction associated with urgency and frequency of stools. From the history, clinical observation, proctoscopic examination, and roentgenologic studies, a tentative diagnosis was established in each case, proved at operation, and immediate relief given by enterocolostomy around the inflammatory mass and colostomy of the transverse colon. Of the four patients, one chose to keep the colostomy and have no further surgery, one was reoperated upon and only closure of the colostomy was done, the third did not desire to keep the colostomy and because the sigmoid continued to be contracted, resection of the sigmoid and short ileal loop was accomplished, followed by closure of the colostomy. The fourth patient later proved to have malignancy of the sigmoid associated with diverticulitis; the perforation could have been secondary to the diverticulum or to the malignancy.

When a fistulous communication develops between the sigmoid and small bowel the ileal fecal material should be prevented from entering the sigmoid and rectum in order to eliminate the symptoms of diarrhea and rectal urgency. This is accomplished by enterocolostomy. Complete diversion by resection of the ileal loops should not be attempted because this might lead to establishment of blind bowel loops which is lethal. The symptomatic condition is relieved and the inflammatory reaction of the diverticulitis of the sigmoid is permitted to subside by establishing colostomy of the transverse colon. Further surgery at a later date is accomplished as indicated by the change in the pathological condition and the wishes of the patient.

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In spite of the rarity of small bowel tumors, it is imperative that we exhaust all ingenuity in elaborating mechanisms referable to diagnosis and treatment. And this is so because we are confronted with the fact that malignancy of the small bowel is an extremely lethal disease.

### ANALYSIS OF CASES

*Incidence*—From the point of view of number of cases, our experience with tumors of the small intestine has been limited. After careful study of our files covering the last fifty years, we have compiled a report on a total of 20 primary tumors of the small bowel; the clinical record on one of these cases is unavailable. Instances of ampullary tumors of the duodenum are omitted from this study because they are probably largely of duct origin. This number represents approximately 1 for every 3,600 surgical and autopsy specimens studied in this hospital. There are in our files records on 1,410 neoplasms of the gastrointestinal tract, from the esophagus, caudal. Thus, small bowel tumors have been encountered at the rate of 1 for every 71 neoplasms elsewhere in the gastrointestinal tract. In spite of this small total number it is interesting to note that 10 of the total of 20 were encountered during the year 1945.

In reviewing the literature on the subject of small bowel tumors, it is evident that our experience is the usual one in that these tumors are conspicuous for their rarity.

*Distribution*—In the 10 cases available for clinical study 13 malignant and 6 benign the distribution between men and women was about equal in each group. The youngest patient having a malignant tumor was 35 the oldest 79 years of age. In the group having benign tumors, corresponding ages were 34 and 66 years. The average age incidence for those in the malignant group was 50 years, the benign group 45 years. Growth of the small bowel probably followed the usual pattern of age distribution for neoplasms generally in that the malignancies occur generally in the fifth and sixth decades, while the benign tumors are more likely to be encountered in the younger. Nevertheless, in the era of cancer consciousness, the trend is to disrespect more and more the traditional age limitations on clinical suspicion regarding malignant neoplasms. We must be even more on our guard inasmuch as given the same histologic malignancy it frequently will progress at a distinctly more rapid pace in a younger than in an older person.

*Duration of Symptoms*—In the malignant tumor group there was no instance of an acute fulminating onset entirely unpreceded by previous complaints. The average duration of symptom here was ten months, varying from one and one-half months to forty-eight months. Further breaking down of this small group revealed that 8 of the 13 patients had symptom for only three months or less. In the group with benign tumors, symptom varied from acute fulminating onset due to sudden intestinal obstruction, to thirty-six months. The average duration of symptoms of those patients with previous complaints was twenty-three months.

*Clinical Symptom and Signs*—In the malignant group the chief complaint was usually pain. This occurred in 9 of 10 patients (90 per cent) of the 13 cases. The pain was usually described vaguely as indigestion with epigastric discomfort or more frequently as periumbilical or lower quadrant intermittent aching. Six of the patients exhibited manifestations of bleeding 4 complained of diarrhea, constipation or intermittence of the two. Weight loss, anorexia, and anemia were present in 11 of the 13 patients. Obvious abdominal habitually detectable manifestations of obstruction and in 5 instances there was a clinically palpable mass.

In the benign group of 6 there were 4 who complained of pain. This pain was usually described as lower quadrant located on no matter which segment of the small bowel was involved. Diarrhea and/or constipation were noted in 4 instances, bleeding in only 1 case. No stercoraceous manifestations were suggested in only 1 case. One half of the patients were obstructed and in one half a mass was palpable.

One cannot describe peculiar clinical patterns for the symptomatology of small bowel tumors. These arise from minor gastro-intestinal distress with poor localization to fulminating pain of acute extraperitoneal obstruction based on fairly sudden occlusion by intraluminal mass or on acute subperception. The dictum that any bizarre intestinal complaints, for which the usual methods of investigation offer no explanation must be forthrightly studied by pertinent x-ray of the small intestine is upheld. One does not have the right to

discharge from observation a patient with persistent, unexplained gastrointestinal complaints without considering and studying the possibility of a small bowel lesion. Additionally if bleeding is present the burden of proof is upon the physician to demonstrate its etiology assuming that the statistically common gastroduodenal and large bowel pathologic entities have been excluded. It has been illustrated that chronic bleeding with a subjective ulcer syndrome in a patient without, and on rare occasions even with x ray manifestations of a gastroduodenal inflammatory lesion may be accountable to a small bowel tumor. In view of the frequently inconclusive x ray findings of small bowel pathology it is perhaps advisable to resort more frequently to exploratory laparotomy.

*X ray Findings*—In 6 instances of malignant and in 3 of benign tumor cases, x ray studies were not done usually because the patient came in with acute obstruction or in extremis. In the 7 remaining malignant tumor cases, obstruction was demonstrable in 4 by radiologic examination. In 1 of these, the obstruction was interpreted as due to neoplasm; in the other 5 there was no postulation as to etiology. Two cases of the 7 studied by x ray examination exhibited what were interpreted as filling defects due to tumor.

In the 3 benign tumors which were subjected to x ray study 1 was registered as a negative examination, 1 as a mechanical obstruction of the ileum and 1 as a filling defect. Generally speaking with regard to tumors of the small bowel x ray studies have been much less satisfactory than those of stomach and colon. Careful serial fluoroscopy and flash films of the small bowel following ingestion of a barium meal are essential and interpretation by a competent radiologist is indispensable. Filling defects, changes in contour, localized paralysis and changes in intraluminal diameters are all requisite points which must be left to the trained eye in all questionable cases. When an obvious extensive carcinomatous filling defect is present, more often than not the anatomic picture is one of a mass which has already extensively metastasized locally and distally. In a few instances, there is one pathognomonic x ray sign corresponding to diffuse infiltrative lymphosarcomatosis of a segment of bowel in a small percentage of cases of bowel lymphosarcoma. Barium studies will demonstrate a picture of a dilated, smooth aneurysmal like sac corresponding to bowel paralyzed by lymphosarcomatous infiltration. Frequently a benign tumor will make itself known clinically and radiologically only when intussusception has occurred.

*Pathology*—An analysis of the types of tumors encountered and of their respective locations and behavior with regard to intussusception is illustrated in Table I. Three neoplasms encountered in the duodenum were all malignant, carcinomas and 1 malignant melanoma. There were none in the first portion of the duodenum. Two of the tumors were perampullary and one was at the duodenojejunal junction. None of the tumors were intussuscepted. This complication did not occur with tumors of the duodenum due to the fixation and immobility of this bowel segment.

In the jejunum 6 tumors were malignant, including 4 carcinomas and 1 lymphosarcoma and 1 was benign. Four of the tumors were in the first portion of the jejunum, 2 in the second and 1 in the third. Of the 6 malignant



*Distribution*.—In the 19 cases available for clinical study 13 malignant and 6 benign, the distribution between men and women was about equal in each group. The youngest patient having a malignant tumor was 35, the oldest 79 years of age. In the group having benign tumors, corresponding ages were 31 and 66 years. The average age in decades for those in the malignant group was 50 years, the benign group 45 years. Growth of the small bowel probably follows the usual pattern of age distribution for neoplasms generally, in that the malignancies occur generally in the fifth and sixth decades, while the benign tumors are more likely to be encountered in the younger. Nevertheless, in the face of cancer consciousness, the trend is to disregard more and more the traditional age limitations on clinical suspicion regarding malignant neoplasms. We must be extremely on our guard inasmuch as, given the same histologic malignancy, it frequently will progress at a distinctly more rapid pace in a young than in an older person.

*Duration of Symptoms*.—In the malignant tumor group there was no instance of an acute fulminating onset entirely unprecedented by previous complaints. The average duration of symptom here was 12 months, arising from one and one-half months to forty-eight months. Further breaking down of this small group revealed that 8 of the 13 patients had symptoms for only three months or less. In the group with benign tumors, symptoms varied from acute fulminating onset due to sudden testicular obstruction, to thirty-six months. The average duration of symptoms for those patients with previous complaints was twenty-three months.

*Clinical Symptom and Sign*.—In the malignant group the chief complaint was usually pain. This occurred in 9 or 70 per cent, of the 13 cases. The pain was usually described vaguely as indigestion with epigastric discomfort or more frequently a periumbilical lower quadrant, intermittent aching. Six of the patients exhibited manifestations of bleeding; 4 complained of diarrhea, constipation, or intermittent relief of the two. Weight loss, anorexia, and anorexia were present in 11 of the 13 patients. On examination, 7 exhibited frank detectable manifestation of obstruction, and in 5 instances there was a clinically palpable mass.

In the benign group of 6, there were 4 who complained of pain. This pain was usually described as lower quadrant in location no matter which segment of the small bowel was involved. Diarrhea and/or constipation were noted in 3 instances, bleeding in only 1 instance. Systemic manifestations were complained of in only 1 case. One-half of the patients were obstructed, and in one-half mass was palpable.

One cannot describe specific clinical patterns for the symptoms and signs of small bowel tumors. These vary from mild gastrointestinal distress with poor localization to a fulminating picture of acute exasperating obstruction based on fairly sudden occlusion by an intraluminal mass or an acute twisting-ception. The dictum that any bizarre intestinal complaint for which the usual methods of investigation offer no explanation must be further studied by patient is always of the small intestine is upheld. One does not have the right to

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In the benign group of 6 there were 4 who complained of pain. This pain was usually lower abdominal lower quadrant in location, no matter which segment of the small bowel was involved. Diarrhea and/or constipation were noted 3 instances, bleeding in only 1 instance. Systemic manifestations were exemplified in only 1 case. On half of the patients were obstructed and in one-half mass was palpable.

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drains the nodes, most of which are situated close to the root of the mesentery. Only comparatively few and small nodes are found along the periphery of the small bowel mesentery at its insertion or in the intermediate zone. In fact rarely only these latter can be included in resection of a bowel segment. The main nodes frequently being situated too close to the large branches of the mesenteric vessel to make the resection of this portion of the mesentery possible. The situation therefore is unfavorable with that encountered in the lymph drainage of the large intestine and may account in some degree for the poor operative result in resection of small bowel for carcinoma.

The sarcomatous tumors apparently all arose from the smooth muscle although all in linked with miniature elements as may be considered to have been of fibrous connective tissue origin. They were represented by a tier well circumscribed, partly encapsulated masses projecting into the lumen. They were attached to the deeper layers of the wall the overlying mucosa usually being compressed in a fold and partly ulcerated. Histologically two types could be differentiated. One comprised a very cellular growth in form composed of closely packed fusiform cells containing round sized (often plump) and hyperchromatic nuclei. Mitotic figures were present and multinucleated tumor giant cells, areas of fat degeneration and necrosis were encountered here. This picture was present in the case in which a tumor tissue metastasis also was present in a regional lymph node. This patient died one and one-half years after operation from all metastatic sarcomatous. The other type found in the remaining cases, presented a similar histologic picture which however was not uniformly found throughout the tumor but mainly in its central portions, the remainder being composed of a well formed mature smooth muscle cell and fibers arranged in a rather orderly fashion in bundles or interlacing strands, supported by a well differentiated fibrous connective tissue stroma. It seems fair to assume that the latter type represent a leiomyoma in which a sarcoma has arisen in contrast to the former where the malignant growth originated directly in the muscularis. It is thus not surprising to find the clinical course of the latter to be benign and these observations find their similarity in the literature where a well differentiated leiomyoma arising in the mesenterium and mesocolon is regarded as a fibroma and followed by similar clinical course, especially if the serosal lymphatics in the small bowel lesion was characterized in every respect. It was situated at the predilection site namely just proximal to the ileocecal valve where anatomically the lymphatic use of the mesocolon is most abundant. Histologically it was of the lymphatic type containing only few reticular cells. Mitotic figures were absent. The neoplasm apparently began as a benign growth which invaded the muscularis but had completely destroyed and replaced the tissue which was well ulcerated. It formed a well developed mass the largest measuring 15 cm. in diameter and occupying the entire jejunal region. The regional lymph nodes were enlarged and contained metastatic lymphosarcoma.

The benign tumors of the operative series encountered in the small intestine were all of the respective histologic groups and histologically appeared as follows:

TABLE I DEMONSTRATING DISTRIBUTION OF TUMOR TYPES, AND FREQUENCY OF INTUSSUSCEPTION IN THIS SERIES OF SMALL BOWEL TUMORS

SMALL BOWEL REGION	PATHOLOGIC TYPES	TOTAL	MALIGNANT REASON	→ INTUSSUSCEPTION MALIGNANT REASON
Duodenum	I		Carcinoma 2 Malignant 1	2 Malignant → 0 Intussuscepted
	II	2		
	III	1		0 Benign → 0 Intussuscepted
Jejunum	I	4		
			Carcinoma 3 Leiomyosarcoma 1	3 Malignant → 1 Intussuscepted
	II	2	Polyp 1	1 Benign → 1 Intussuscepted
			Adenocarcinoma 1	
	III	1		
Ileum	I	5		
			Carcinoma 1 Leiomyosarcoma 1 Spindle cell sarcoma 1 Leiomyosarcoma 1	4 Malignant → 2 Intussuscepted
	II	6		
			Fibroma 4 Lipoma 4 Leiomyoma 1	6 Benign → 2 Intussuscepted
	III			
			Lymphosarcoma 1	
			Adenocarcinoma 1	
			Lymphosarcoma 1	
		20		13 Malignant → 3 Intussuscepted 7 Benign → 4 Intussuscepted

tumors, 1 produced an intussusception, and the single benign tumor also was intussuscepted.

In the ileum, 4 malignant tumors were recorded 1 each of carcinoma, lymphosarcoma, spindle-cell sarcoma, and leiomyosarcoma and 6 benign tumors, namely 4 fibromas, 1 lipoma, and 1 benign leiomyoma. Two of the tumors were in the first portion of the ileum in the mid portion, and 6 in the terminal, third. Of the 4 malignant tumors, were complicated by intussusception.

majority are located near the beginning or the end of the small intestinal tube. Of the total 13 malignant tumors, only 3 were complicated by intussusception, whereas 4 of the total 7 benign tumors of the small bowel were intussuscepted.

The malignant neoplasms of epithelial origin were all of the adenocarcinomatous type. All more or less projected into the lumen, one constituting large cauliflower like mass. On microscope examination all had infiltrated the muscularis but in only one was the serosa infiltrated and penetrated. At operation lymph node metastases were demonstrable in every case of adenocarcinoma. The lymph from the small intestine is collected in a suberosal plexus and

trains to the nodes, most of which are situated close to the root of the mesentery. Only comparatively few and small nodes are found along the periphery of the small bowel mesenter at its insertion or in the intermediate zone. Unfortunately only these latter can be included in resection of a bowel segment, the main nodes frequently being situated too close to the large branches of the mesenteric vessels to make the resection of this portion of the mesentery possible. This situation therefore differs unfavorably with that encountered in the lymph drainage of the large intestine and may account in some degree for the poor operative results in resection of small bowel for cancerous disease.

The carcinomatous tumors apparently all arose from the smooth muscle although all included an immature element which may be considered to have been of fibrous connective tissue origin. They were represented by rather well-encapsulated partly encapsulated masses projecting into the lumen. They were attached to the deeper layers of the wall the overlying mucosa usually being depressed, in addition partly ulcerated. Histologically two types could be differentiated. One comprised a very cellular growth with a cellular composition of closely packed to a certain extent anastomosing variably sized, often plump and hyperchromatic cells. Mitotic figures were present and multilayered tumor giant cells were present. In the degeneration and necrosis were encountered here. This picture was present in the case in which a tumor of the metastatic type was present in a lymph node. The patient died nine and one-half years after operation primarily of metastatic carcinomatous disease. The other type found in the remaining cases presented a similar histological picture which however is not uniform found throughout the tumor but mainly in its central portions the remainder being composed of poorly formed mature smooth muscle cells and fibers arranged in a rather orderly fashion as bundles or interlacing strands supported by a well-differentiated fibrous connective tissue stroma. It seems fair to assume that the latter type represents a lesion in which a carcinoma has arisen in contrast to the former where the malignant growth originated directly in the muscularis. It is thus not surprising to find the clinical course of the latter to be benign and these observations find their similarity in the uterus where a similar difference in the stroma arising in the myometrium and the arising in the fibrous stroma followed by similar clinical courses respectively. In the case of the fibrosarcoma the small bowel lesion was characterized in every respect. It was situated in the predefect site namely just proximal to the ileocecal valve where anatomically the lymphatics of the mucosa enter the submucosa. Histologically it was of the lymphocytic type consisting mainly of small reticular cells. Mitotic figures were absent. The neoplasm apparently slow growing had only slightly invaded the muscularis but had completely destroyed and replaced the mucosa which was well ulcerated. It formed several polypoid masses the largest measuring 1.8 cm in diameter and causing the intussusception. The regional lymph nodes were enlarged and extensive invasion by lymphomatous cells.

The benign nature of the connective tissue series encountered in the small intestine was in every respect characteristic gross and histological appearance.



TABLE I. DEMONSTRATIVE DISTRIBUTION, PATHOLOGIC TYPES, AND FREQUENCY OF INTUSSUSCEPTION IN THIS SERIES OF SMALL BOWEL TUMORS

SMALL BOWEL SEGMENT	PATHOLOGIC TYPES	TOTAL	MALIGNANT RESECTION	→ INTUSSUSCEPTORY MALIGNANT RESECTION
Duodenum	I		Carcinoma 2 M leiomyosarcoma 1	3 Malignant → 0 Intussuscepted
	II	2		
	III	1		0 Benign → 0 Intussuscepted
Jejunum	I	4		
	II		Carcinoma 5 Leiomyosarcoma 1	6 Malignant → 1 Intussuscepted
	III	1	Polyp 1	1 Benign → 1 Intussuscepted
Ileum	I	5		
			Carcinoma 1 Leiomyosarcoma 1 Spindle cell sarcoma 1 Leiomyosarcoma 1	4 Malignant → Intussuscepted
	II	5		
		6		
			Fibroma 4 Lipoma 4 Leiomyoma 1	6 Benign → 3 Intussuscepted
	III			
		20		13 Malignant → 5 Intussuscepted 7 Benign → 4 Intussuscepted

tumors, 1 produced an intussusception, and the single benign tumor also was intussuscepted.

In the ileum, 4 malignant tumors were recorded: 1 each of carcinoma, lymphosarcoma, spindle-cell myosarcoma, and leiomyosarcoma and 6 benign tumors, namely 4 fibromas, 1 lipoma, and 1 benign leiomyoma. Two of the malignant tumors of the ileum had intussusception as a complication, and 6 in the benign group had intussusception as a complication.

In summation, one-half of the neoplasms were located at the extremities of the jejunal ileal segment. This is also the statistical fact in large collected series of small bowel tumors, in that the majority are located near the beginning or the end of the small intestinal tube. Of the total 13 malignant tumors, only 3 were complicated by intussusception, whereas 4 of the total 7 benign tumors of the small bowel were intussuscepted.

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operation and the other one and one-half years. Suffice to say the 3 patients who were not operated upon died shortly after admission.

In the group with benign tumors one patient died six months after operation of metastases from an antecedent carcinoma of the cervix. Two died in the postoperative period of surgical complications, one, with a submucous fibroma of the ileum with intussusception, died on the third postoperative day of pneumonia. A second died suddenly on the fourth postoperative day following ileocecal resection for leiomyoma of the ileum with obstruction. The 3 remaining patients underwent uneventful recoveries and are surgically well.

None of the patients in the group having benign tumors died because of the intestinal neoplastic disease. On the other hand, all patients with carcinoma succumbed because of the intrinsic malignant disease. The outlook for lymphosarcoma of the small bowel is probably about the same as of carcinomas. In this group only those with leiomyosarcoma survived, establishing the fact that with the present treatment of malignancies of the small bowel, the over-all prognosis is extremely discouraging.

#### REVIEW OF THE LITERATURE

In the past several years, the literature has been fairly replete with reports on small bowel tumors. A review of a few of the more comprehensive surveys is in order at this juncture.

The impetus for study and classification of small bowel tumors was provided in exhaustive and painstaking surveys contributed by Raiford in 1932 and 1933. He reviewed in exquisite detail descriptions of 88 tumors of the small bowel recorded in the surgical pathology files at the Johns Hopkins Hospital. The small bowel tumors comprised 89 per cent of all gastrointestinal tumors. Of all benign gastrointestinal tumors 23.8 per cent and of all malignant tumors of the gastrointestinal tract 4.9 per cent were in the small bowel. In his cases, 37 per cent gave symptoms sufficient to warrant operation. 17 per cent had uncertain symptoms, were not operated upon and the tumor was found at autopsy. 46 per cent had no symptoms, and the growth was discovered accidentally at autopsy.

Cave in 1932 reported on 14 small bowel tumors at Roosevelt Hospital. He classified the benign tumors into lipomas, myomas, adenomas, carcinoids, hemangiomas, fibromas, pancreatic rests, and cysts. Carcinoma was the most common of the malignant tumors. He emphasized the investigation of early nondescript mild gastrointestinal complaints.

Duodenal malignancies are dealt with in a recent publication by Dixon and associates. They demonstrated that diagnosis here is somewhat facilitated in contrast to similar lesions in the jejunum and ileum because of the changes in clinical physiology produced by expanding lesions compressing or occluding the duodenum, the pancreatic system or the biliary system. Consequently roentgenologic examination was relied upon earlier as patient were driven to medical consultation by manifestations of obstruction, bleeding, jaundice or pain. Roentgenologic evidence of obstruction in the second or third portions of

The only benign tumor of epithelial origin was an adenomatous polyp in the jejunum; it measured 5 cm in diameter and was attached to the mucosa by a narrow pedicle measuring 5 cm in length. Due to the intussusception the tumor was extensively hemorrhagic.

*Operative Procedure*.—In the group of malignant tumors, 3 of the 13 patients were not operated upon: one was admitted in uremia, another in extremis, and a third had had a radiagnosis of a retroperitoneal tumor and had been treated with deep x-ray therapy. Primary resection was done with immediate anastomosis in eight instances. In one case a perampullary lesion in a patient who had been operated on twenty-six days before and at which time a cholecystectomy and a choledochotomy had been performed was biopsied at a subsequent laparotomy performed because of massive hemorrhage through the choledochotomy T-tube tract. Local excision with the cautery was resorted to in the case of the duodenal melanoma, adjacent to the ampulla.

All 6 benign tumors were resected, de-to-sul anastomosis being done in 5 cases and end-to-end in 1 case.

The treatment of lesions of the duodenum, malignancy in particular, is undergoing a revolutionary change. With the newer concepts of cholangio-pancreatoduodenal physiologic and surgical anatomy as initially elaborated and practiced by Whipple over ten years ago, massive resections for previously regarded hopeless conditions are now entering the stage of practicability. In the jejunum, segmental resection including corresponding mesentery to its root is the obvious procedure. Nevertheless, the anatomic picture is usually one of distant dissemination at the time of resection.

When an intussusception is encountered at operation, the situation is handled in the standard manner. If reduction cannot be easily accomplished because of the bulk of the tumor the intussuscepted mass must be resected in toto. If inseparable adhesions between intussusceptum and intussusceps are present, the treatment is similar. Should the reduced intussusceptum exhibit alterations which lead one to suspect that mural vascular insufficiency is established, then one should include this region in the resection.

*Recorded Results*.—Regarding results of the 10 malignant tumors operated upon, there were 3 deaths attributed to the immediate postoperative period. 1 patient died on the first postoperative day of shock, second on the fifth post-

after extensive resection for an adenocarcinoma of the jejunum; this patient had been carried along

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*Recorded Results*—Regarding results of the 10 malignant tumors operated upon, there were 3 deaths attributed to the immediate postoperative period: 1 patient died on the first postoperative day of shock, a second on the fifth postoperative day of lobular pneumonia, and the third on the day of operation from shock following a heroic attempt which was made to resect the duodenojejunal junction and a large metastatic mass circumscribing the superior mesenteric artery. Four patients died of metastases three months, eighteen months, nineteen months and twenty months, respectively, following resection. One patient with diffuse ileocecal and rectal sarcomatosis was living and well eighteen months after extensive resection for an ileocecal intussusception secondary to a pedunculated ileal lymphosarcomatous tumor; this patient had been carried along very favorably with deep x-ray therapy. At the time of this writing, the only patients in this group living and entirely free of evidences of recurrence are the 2 in whom the tumor was a leiomyosarcoma. One of these was beyond

X-ray diagnosis of small intestinal malignancies was reviewed by Swenson in 120 cases. Usually the patient did not present himself until obstructive symptoms had occurred. X-ray qualities were reviewed in terms of size and shape of the small bowel lumen, contour and pattern of its walls, and the effect of the tumor on the motility of the bowel. Serial half hour roentgenograms were stressed. In the discussion of this review Ros Golden pointed out that in the differential diagnosis, the lesion produced by a carcinoma or carcinoid is small, short 4 to 6 cm in length, whereas an inflammatory lesion is usually considerably longer.

Gastrointestinal smooth muscle tumors were reviewed by Gillen and Stout in an excellent analysis of the literature of the entire subject of leiomyomas of the gastrointestinal tract. They demonstrated the paradox of the classification of these tumors into benign and malignant illustrating that frequently poorly differentiated histologically malignant tumors do not behave so innocently while occasionally infiltrative and metastases are subsequently exhibited by a histologically well-differentiated tumor. They also discussed the confusion encountered in differentiating these tumors from other connective tissue tumors, particularly the neurilemmoma.

A word might also be added concerning carcinoid tumors. Many reports in the literature regard these basal cell tumors of the intestinal wall as entirely benign. This is not always the case. Several reports are available of unquestioned removal of the small intestine, the appendix, or the cecum, which have metastasized to regional nodes and on to the liver.

Thirty-five cases of benign small intestinal tumors at the Mayo Clinic were reported in 1933 by Rankin and Newell. In order of frequency these included adenomas, lipomas, fibromas, lymphomas, hemangiomas, submucous adenomas, adenomyomas, and ulcerous osteochondroma. Eighteen of the cases included symptoms and in 11 the tumor was encountered incidentally at laparotomy. Symptoms were essentially those secondary to intussusception, progressive intestinal obstruction, and hemorrhage. They observed that the most common single cause of intussusception in adults is a benign tumor of the small intestine.

Regarding lipomas of the gastrointestinal tract there have been few significant contributions to the subject since the classical review in *The Submucous Lipoma of the Gastrointestinal Tract* by Hiltner in 1909. Behrstedt<sup>11</sup> reviewed the literature in 1943 with emphasis on the subject of intussusception and added 6 of his own cases.

The subject of obscure gastrointestinal hemorrhage has lately and rightfully been receiving more attention in the literature. Baker and Halley reported cases of small intestinal neurofibroma with long-standing recurrent episodes of tarry stools in the presence of otherwise good health. In each case suspicion of ulcer existed but the instituted ulcer management was followed by a recurrence of the bleeding. They further present a review of the interrelationships of fibroma, neurofibroma, and myofibroma and demonstrated the difficulty in histologically distinguishing these at times.

the duodenum makes it expedient to consider neoplasia as a diagnostic possibility. They discussed recent advances in operative approaches, and cited a case of duodenal adenoma which was resected two years after it had been identified at a previous operation. They concluded that the prognosis is better with duodenal neoplasia than with neoplasia in the jejunoileal segment because earlier symptoms are laborated, and the mass impinges upon adjacent stomach or upon other parts both of the two duet.

In 1948 Donohue and Jones reported primary small intestinal malignancies. Malignant tumors of the duodenum are reviewed; ileal and ileocolic diseases classified according to position upon the small intestine resulting in pyloric obstruction, periaampullary tumors resulting in obstructive jaundice, and intra-ampullary tumors resulting in distention with bile stasis. Carcinomas are described in terms of constitutional symptoms and the regional symptoms secondary to (1) acute obstruction usually due to intussusception and (2) gradual obstruction by the tumor with slow progressive obstruction. Sarcoma of the ileum and jejunum is discussed. The occasionally seen pathognomonic x-ray picture of localized aneurysmal dilatation of a small segment of bowel due to diffuse mural infiltration is reviewed. These authors quoted Munn as noting that 60 per cent of intestinal sarcomas are situated in the small bowel.

Cameron gave an excellent concise review of the clinical pathology of primary malignancies of the jejunum and ileum. He reported 4 fatal cases out of 196 simulated from the literature. He noted that adenomas and sarcoma of the small bowel are almost equally in incidence and that malignant carcinomas comprise 6.5 per cent of the mechanical obstruction is caused by 80 per cent of adenomas and by 50 per cent of sarcomas and that diagnosis is frequently impossible without necropsy. His conclusions are indicated that in one fifth of the cases the diagnosis is correctly made, two-thirds of the cases operable though the mortality being 90 per cent and five-year survival less than 10 per cent.

In a review of intestinal lymphomas, Usher and Dixon offered indices on prognosis for small bowel lymphosarcomas. They found that the average survival was nine months as contrasted to two years for lymphosarcomas of the rectum and sigmoid. As for lymphosarcoma of the cecum. All but one of the 19 patients operated upon for lymphosarcoma of the small bowel died of recurrence within one year. They reported on 60 cases of intestinal lymphosarcoma with 38 per cent located in the small bowel. Reticular cell sarcoma and malignant lymphocytoma (small round-cell sarcoma) are distinguished.

Melanoma of the small intestine is usually regarded as a pathological rarity. Hirsch and Manges reported on 3 cases and noted 3 others in the literature. They reviewed convincing evidence that melanoma of the small bowel, perhaps all malignant tumors, even when the primary tumor is not evident, in our case because often the fact of a previously removed small intestine is not well known or permission to resect in the event of postoperative pain is undoubtedly

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In 1936 Doull and Jones reported on primary small intestinal malignancies. Malignant tumors of the duodenum are reviewed in detail and clinical diagnoses classified according to position on the small intestine: ampullary tumors resulting in pyloric obstruction, perampullary tumors producing obstructive jaundice and ileo-ampullary tumors resulting in obstruction with distention. Carcinomas are described in terms of constitutional symptoms and the regional symptoms secondary to (1) acute obstruction usually due to intussusception, and (2) gradual occlusion by the tumor with slow progressive obstruction. Carcinoma of the ileum and jejunum is discussed and the occasionally seen pathognomonic ray plot is of localized antral dilatation of small segment of bowel due to diffuse mural infiltration is reviewed. These authors quoted Jones as noting that 65 per cent of testicular sarcomas are encountered in the small bowel.

Cameron gave an excellent concise review of the clinical pathology of primary malignancies of the jejunum and ileum. He reported on 4 of his own cases and in 196 accumulated from the literature. He concluded that carcinomas and sarcomas of the small bowel are nearly equal in incidence and that malignant carcinoid comprise 65 per cent of that mechanical obstruction is caused by 80 per cent of carcinomas and by only 50 per cent of sarcomas so that diagnosis is frequently impossible in nonobstructive cases. His accumulated figures indicated that in one-sixth of the cases clinical diagnosis correctly made two-thirds of the cases operable though the mortality being 30 per cent and the five year survival less than 10 per cent.

In a review of testicular lymphosarcomas Lisher and Dwyer offered statistics on prognosis for small bowel lymphosarcomas. They found that the average survival was nine months as compared to two years for lymphosarcoma of the rectum and eight years for lymphosarcoma of the stomach. All but one of the 19 patients operated upon for lymphosarcoma of the small bowel died of recurrence within one year. They reported on 50 cases of testicular lymphosarcoma with 39 per cent located in the small bowel. Reticular cell sarcoma and malignant lymphoma (small round cell sarcoma) are listed as benign.

Melanoma of the small intestine is usually regarded as a pathologic curiosity. Herbut and Manges reported on 5 cases and noted 13 others in the literature. They reviewed on the generalities that melanoma of the small bowel is perhaps always a metastatic tumor even when the primary tumor is not evident as in our case because often the first of the primary removed malignant lesion is not made known or permission to resect the first post-operative examination is obtainable.

carefully during the next forty eight hours during which he seemed to experience complete remission as the complaints of pain and stool were passed. On the third day crampy pain recurred and on physical examination there was no distention, but for the first time there was noted a loop type succession splash on rocking the patient and on direct auscultation. No visible peristaltic waves were demonstrable and sounds are not excessive in any of the abdominal quadrants. A gastrointestinal series taken at this time exhibited several loops of small bowel which were perceptibly distended. At forty four hours the barium was distributed irregularly from the cecum to the sigmoid. The findings were interpreted as characteristic of partial mechanical small bowel obstruction.



Fig. 1—Intussusception secondary to leiomyosarcoma of ileum. The obstructed loop of ileum in the left upper quadrant is localized. The black rectangle on this and the arrow show the midline corresponding to the intussuscepted segment, and below the region of free distribution of barium (peristaltic) prevent the intussusception from the intussusception and intussusception.

Laparotomy was performed 11 days following admission. A small bowel obstruction present. This was caused by intussusception 18 cm. segment of upper ileum. The intussusception was readily reduced by gentle taxis. All involved bowel and mesentery appeared viable. The per of the intussusception as formed by pedunculated, firm, intraluminal tumor the size of small pea there as dimpling of the serosa corresponding to the tumor. Two enlarged hard lymph nodes were noted at the base of the mesentery in the drainage field of the tumor. A block resection of generous segment of ileum with wedge of corresponding mesentery extending to its root was done and side to side enterostomy performed. The patient made an uneventful recovery and prior to discharge two weeks after operation repeat gastrointestinal series was interpreted as there is still some dilatation of one of the loops of small intestine apparently proximal to the enterostomy; the amount of distention is considerably less marked than on the previous examination.

The tumor was pedunculated leiomyosarcoma the enlarged nodes included in the resection are extensively inflamed but contained no metastatic deposits.

Smith and associates reported 3 cases of small intestinal tumor as a cause of recurrent melena at the Mayo Clinic. They called attention to the fact that in cases of ulcer type pain a demonstrable deformity in the duodenal bulb, and a history of melena, two lesions may be present and the melena may be from a coexistent tumor of the ileum or jejunum. Difficulties of x-ray diagnosis are pointed out. The expense and time involved in small bowel serial x-ray views sometimes are great, and at that, not all lesions are by any means demonstrable. However such examination is indicated when no lesion is found in the rest of the gastrointestinal tract to explain bleeding or where it appears probable that the known lesion is not the source of the bleeding. They offered interesting statistics: in a review of the cases of bleeding there were 968 sources of bleeding found in the stomach or duodenum for every one found in the small intestine beyond the duodenal bulb. A relatively small number of instances of melena are the result of tumors of the jejunum or ileum, but the incidence of bleeding from tumors in this area is very high.

Segal and his co-workers also wrote on lesions of the small intestine producing massive hemorrhage. They noted that the combination of postprandial pain and melena being produced by lesions in the small intestine beyond the duodenum has not been stressed in the literature. They reported on 3 patients with such lesions, 2 of whom had repeated hospital admissions, each time being treated for bleeding duodenal ulcer. They reviewed other similar cases in the literature and suggested in detail added diagnostic measures. T. E. Jones, in the discussion with the article, made a plea for early exploratory operation in all cases of exsanguinating hemorrhage even though the x-ray findings are consistently negative.

#### CASE REPORTS

All cases are graphically analyzed in Table II. Two of these are noted here in more detail. The one, a case of leiomyosarcoma of the ileum with chronic intussusception in a young adult illustrates pertinent features in regard to the behavior of this group of tumors from the point of view of clinical and radiologic diagnosis, treatment, and result. The second case of spontaneous ileocolostomy secondary to primary carcinoma of the ileum demonstrates the late stage at which the patient is frequently seen in consultation for the initial time and additionally substantiates the guarded prognosis which carcinoma of the small intestine bears.

CASE 1.—T. K., 22-year old white man, clerk, was admitted to the hospital with the complaint of mild abdominal rumblings and short episodes of crampy pain for two months. For five days prior to admission the pain was noted more frequently was accompanied by some nausea, and the patient had vomited several times during the four days prior to admission and three times on the day of admission. He claimed to be able to pass flatus freely. There was no history of diarrhea or constipation, no bloody or tarry stools, no jaundice. The remainder of the history was uncontributory. On physical examination the patient did not appear chronically or acutely ill. Pulse and temperature were normal. Examination of the abdomen revealed entirely negative findings except for mild tenderness just below and to the left of the umbilicus. No mass was palpable. Auscultatory sounds were normal. Rectal examination was negative except for the presence of a small hemorrhoid. The white blood count was 8,000, with normal distribution. The patient was observed

carefully during the next forty eight hours during which he seemed to experience complete remission of the complaints; flatus and stool were passed. On the third day crampy pain recurred and on physical examination there was no distention, but for the first time there was noted loop type succussion splash on rocking the patient and on direct auscultation. No visible peristaltic waves were demonstrable and sounds were not excessive in any of the abdominal quadrants. A gastrointestinal series taken at this time exhibited several loops of small bowel which were perceptibly distended. At twenty four hours the barium was distributed irregularly from the cecum to the sigmoid. The findings were interpreted as characteristic of a partial mechanical small bowel obstruction.



Fig. 1.—Intussusception secondary to leiomyosarcoma of ileum. The obstructed loop of ileum is the left per. quadran. (indicated). The blank area between the arrow and the midline corresponds to the intussuscepted segment. And here the region of free distribution of barium (peripherally) is present in the terminal ileum even the intussusception and ileocecal junction.

Laparotomy was performed 31 days following admission. A small bowel obstruction was present. This was caused by intussuscepted 15 cm segment of upper ileum. The intussusception was readily reduced by gentle taxis. All involved bowel and mesentery appeared viable. The per. of the intussusception was formed by pedunculated firm, intraluminal tumor the size of a small prune; there was dumping of the ileum corresponding to the tumor. Two enlarged hard lymph nodes were noted at the base of the mesentery in the drainage field of the tumor. A block resection of generous segment of ileum with wings of corresponding mesentery extending to root was done and side to side enterointerostomy performed. The patient made an uneventful recovery and prior to discharge two weeks after operation repeat gastrointestinal series was interpreted as there is still some dilatation of one of the loops of small intestine apparently proximal to the enterointerostomy. The amount of distension is considerably less marked than on the previous examination.

The tumor was pedunculated leiomyosarcoma; the enlarged nodes included in the resection were extensively inflamed but contained no metastatic deposits.

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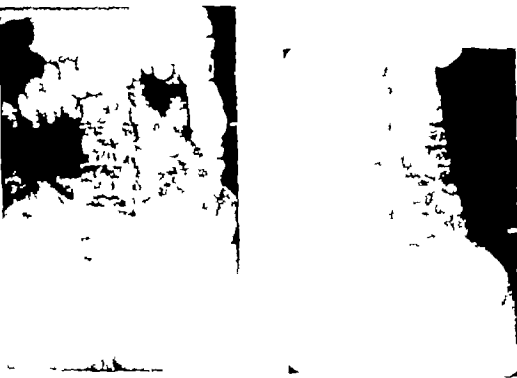


TABLE II—Cont.

CASE	AGE	SEX	TIME OF SYMPTOMS	PRE-EXISTING SYMPTOMS	BLEEDING	PALPABLE MASS	OBSTINATE	EXTRA PERITONEAL	PERITONEAL DISSEMINATION	P. THOUGHT AT OPER. THAT ORIGINARY	OPERATIVE PROCEDURE	OUTCOME OR FOLLOW UP
11 1913	24	F	6 weeks	Crampy abdominal pain, constipation, nausea and vomiting	N	N	Yes	Menstrual, disordered, and junctional dilatation reducing complete obstruction 6.5 cm. from ligament of Treitz	Intestinal obstruction	Unoperated	Holotomomy of jejunum, resection of jejunum, and ileo-ileostomy anastomosis	Unsuccessful recovery and died after 2 wks.
12 1914	29	F	4 yr	Bleeding, severe abdominal pain in upper quadrants, constipation and shock	N	N	Yes	—	Stricture of small bowel	Polyp of jejunum with nonresectable intramural obstruction	Resection of intramural jejunum and ileum and ileo-ileostomy anastomosis	Died 6 mos. later of metastases from antecedent carcinoma of cervix
13 1914	26	F	1 mo	Hypertensive vomiting, herry stools, weight loss	Yes	N	Yes	Partial adhesion of mid-jejunum with filling of feet, probably mesoperium	Intestinal obstruction secondary to tumor	Carcinoma of mid-jejunum with obstruction and nodal metastases	Resection of jejunum and ileum and ileo-ileostomy anastomosis	Died 7 mos. later metastases 20 mos. later
14 1915	44	M	15 mos.	Bleeding, diarrhea, weight loss, crampy lower abdominal pain	Yes	Yes	Yes	Intestinal obstruction secondary to the mid-transverse colon spread secondary to polypoid lymphatic sarcoma of masses of ileum, and lymphatic carcinoma of colon and of mesenteric nodes	Intestinal obstruction secondary to the mid-transverse colon spread secondary to polypoid lymphatic sarcoma of masses of ileum, and lymphatic carcinoma of colon and of mesenteric nodes	Resection of intestine and ileo-ileostomy anastomosis	Intestinal resection three courses of ray therapy ad is ultimately short evidence of disease 18 mos. P.O.	

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careful examination of the mounted junctions of all members of the lesion has been performed in order for the lower shown with b, b' and d become adherent to and located through adjacent lower enamel plates and in irregularities, and in no small region has dislodged plates resulting in its intercalation.



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following initial resection the patient was carefully examined in routine checkup and was found to be entirely well. However seventeen months postresection the patient returned from position in Maine with the history of weakness, anorexia, cough, and weight loss for one month. Findings are reflective of disseminated peritoneal and cervical lymph and carcinomatous. The patient was admitted to the hospital and died of the malignant condition within two months of onset of symptoms of recurrence and within eighteen months following resection.

The original barium enema studies on this patient are demonstrated in Fig. 1.

# SUMMARY AND CONCLUSIONS

A careful survey has been made of all the material on tumors of the small bowel in the past forty years in a large voluntary hospital. Representative works in the literature on the subject are reviewed. Two cases of malignancy of the small bowel, one a leiomyosarcoma of the ileum in a young adult and the other an adenocarcinoma of the ileum ulcerating into the descending colon, are presented in detail to demonstrate the problems which malignant neoplasms of the small bowel involve.

This study on a small group of cases substantiates the experiences of others who have encountered and treated neoplasms in these portions of the gastrointestinal tract. Tumors of the small bowel are conspicuous in their rarity. But concerning the benign group, it may be said that there exists no more elusive a group of lesions. With regard to the malignant group there are few malignant neoplasms which are more lethal, at least as applied to the carcinomas. Therefore these lesions must be kept in mind by the clinician and the surgeon in the analysis of any vague gastrointestinal complaints in any age group or in the investigation of obscure gastrointestinal bleeding. A particular symptom complex simply does not exist. Additionally even the carefully planned radiologic investigation may be unconvincing in establishing a diagnostic interpretation leading to the conviction of the existence of a small intestinal neoplasm. Therefore, because of these latter facts and because of the present status of minimal risk involved in elective abdominal surgery one is led to feel that laparotomy should be resorted to more frequently in those instances where exhaustive diagnostic studies leave one in doubt.

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following initial resection the patient was carefully examined as routine checkup and was found to be entirely well. However seventeen months postresection the patient returned from prison in Manila to the history of weakness, nausea, cough, and weight loss for one month. Findings were reflective of disseminated peritoneal and cervical lymph node carcinomas. The patient was admitted to the hospital and died of the malignant condition within two months of onset of symptoms of recurrence and within eighteen months following resection.

The original biopsy cases studies on this patient re demonstrated (Fig. 2).

#### SUMMARY AND CONCLUSIONS

A careful survey has been made of all the material on tumors of the small bowel in the past forty years in a large voluntary hospital. Representative works in the literature on the subject are reviewed. Two cases of malignancy of the small bowel—one a leiomyosarcoma of the ileum in a young adult and the other an adenocarcinoma of the ileum ulcerating into the descending colon, are presented in detail to demonstrate the problems which malignant neoplasms of the small bowel involve.

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## PANCREATIC CYST

### INTERNAL DRAIN UTILIZING THE ROUX PRINCIPLE

ANTHONY V. MIGNACCIO, M.D. AND EDWARD C. LATHROP, M.D.  
PROVIDENCE, R. I.

ADAMS and Nishijima<sup>1</sup> recently reviewed the literature on pancreatic cysts and presented the experiences of the Lahey Clinic with nine cases which entered there in the last twenty years. Six of these cases were pseudocysts, two were papillary exfoliant adenomas, and one was a hemorrhagic cyst.

They prefer internal drainage to marsupialization. This is accomplished by carrying a loop of jejunum through the transverse mesocolon and anastomosing the jejunum to the cyst wall and then they perform a jejunojejunostomy to divert the intestinal stream.

Utilization of the Roux principle seems a more logical way to accomplish internal drainage. It gives us a long arm which drains the pancreatic cyst. The peristaltic waves in this arm will help, if not prevent the contamination of the cyst by food particles in a greater percentage of cases than can be expected from the loop technique.

This principle was utilized in the treatment of the following case.

M. R. is seen at the Rhode Island Hospital, April, 1947. He gives history of long standing symptoms of gall bladder disease for years. A recent episode is treated by cholecystectomy June 14, 1946. Two weeks later follow-up examination shows the patient suffered from three attacks of acute pancreatitis. He is hospitalized, but he noted some swelling in the epigastrium. The swelling increased gradually until he came to the hospital for treatment (see Fig. 1).

He had no history of alcohol intake and no past history of gall stones. There was no history of pressure on the upper abdomen. There had been no vomiting or loss of weight. There was constipation at times.

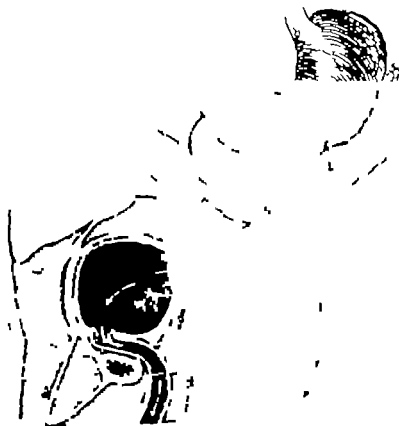
Except for the visible distention of the epigastrium extending over to the left hypochondrium, there were no significant findings except for the roentgenogram, taken April 17, 1947, which showed the shadow of a large, rounded soft tissue mass in the upper midabdomen probably due to pancreatitis. At the time of admission the mass was sharply delineated but the upper margins were obscured by the liver and other soft tissue structures. No definite calcification was seen. Bowel shadows were normal in size, position and outline. The stomach and other soft tissue structures appeared normal. The colon was displaced downward and forward by the mass. There were no signs of intestinal obstruction.

The diagnosis of pancreatic cyst was made and surgery was planned. On April 1, 1947, operation was performed for internal drainage of the pancreas was carried out using the Roux principle. The jejunum was brought up to the abdomen and anastomosis was made to the cyst wall and then the jejunum was anastomosed to the jejunum. The incision was carried across the midline and part of the left rectus abdominis muscle was closed.

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Fig 1—Specimen showing marked fullness in the upper portion.



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Fig 2—The large specimen in the lower part of the figure is the specimen of the pancreas, showing the cystic duct and the main pancreatic duct. The specimen is shown in the lower part of the figure, showing the cystic duct and the main pancreatic duct. The specimen is shown in the lower part of the figure, showing the cystic duct and the main pancreatic duct.





Fig. 1—Photograph shows a dark, irregular mass (likely a pancreatic cyst) in the upper abdomen, with a white, fibrous structure (likely the stomach) visible below it.

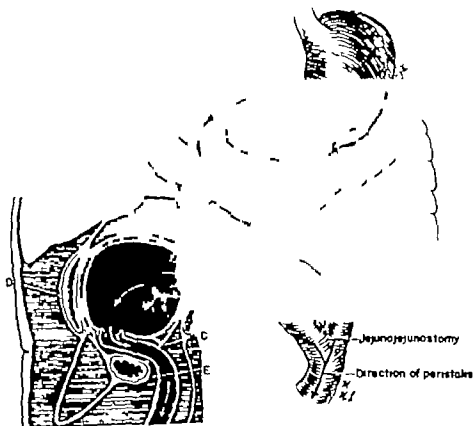


Fig. 2—The large, dark, irregular mass (likely a pancreatic cyst) is shown in the upper abdomen. The stomach (D) is shown below it. The jejunum (E) is shown to the right of the mass. A dashed line indicates the direction of peristalsis. A small inset shows a cross-section of the jejunum with a 'J' shaped incision, labeled 'Jejunojejunostomy' and 'Direction of peristalsis'.

reared so as to obtain adequate exposure. The stomach was fattened out. The cyst was very large and measured approximately six to eight inches in diameter. It was very tense. The cyst was then dissected free from the posterior wall of the stomach, after it had been approached through an opening in the gastrocolic omentum, thus exposing enough of the cyst. It was secured in part using the anastomosis. The cyst was then opened, and approximately 1100 cc of dark brown fluid were removed by suction. The Ligament of Treitz was identified. Approximately six inches below this point the jejunum was transected. The distal end was carried through an vascular portion of the transverse mesocolon, and an open anastomosis was carried out between the jejunum and open end of the jejunum using outer row of O-silk mattress suture and an inner row of N 00 extra hard chromic silk lock stitch posteriorly and Connell anteriorly. The anastomosis seemed to be quite firm and satisfactory. The cut end of the proximal jejunum was then sutured to the distal limb of the jejunum approximately six inches below the point of anastomosis of the jejunum to the cyst. This was an end to side anastomosis, using the open technique and mattress sutures of O-silk on the outer layer and N 00 chromic extra hard on the inner layer. The wound was then closed in layers using N 00 double continuous in the peritoneum and also posterior fascia, N 0 chromic mattress in the fascia and muscle, N 0 chromic interrupted in the fascia, and interrupted silk in the skin. (See Fig 2.)

The convalescence in this case was uneventful. The patient was out of bed on the second day and home on the eighth day.

During the first twenty-four hours gravity drainage with Levine tube was instituted. Nothing was given by mouth for forty-eight hours, and then sips of water were allowed for the next forty-eight hours. Following this fourth day Balfour diet was used with the usual progression. On the seventh day the patient tolerated soft diet well and he was kept on this for another week. After this period regular house diet was advocated. Six weeks after the operation the patient had already gained twelve pounds. He enjoyed the food and had no symptoms of any kind.

The enlargement noted in the upper abdomen disappeared on the operating table and did not recur.

It is obvious that no sound and valid conclusions can be drawn from the result obtained in this case but it is felt that this case can be used as evidence of the evidence that internal drainage of pseudo-cyst of the pancreas is the procedure of choice over marsupialization. It is the hazards of prolonged drainage skin irritation.

Moreover adoption of the Roux principle of drainage of pancreatic cysts is advanced as being preferable to the use of a loop of jejunum with a jejunojejunostomy.

#### SUMMARY

1 Internal drainage of pancreatic cyst is advocated.

The Roux principle seems to offer more chance of eliminating contamination of the site than does the use of loop of jejunum with a jejunojejunostomy.

3 A patient successfully treated by utilizing the Roux principle is reported upon.

## CHRONIC INFLAMMATORY INTESTINAL OBSTRUCTION DUE TO *ENTEROBIUS VERMICULARIS*

JOSEPH M. MILLER, M.D. AND MILTON GINSBERG, M.D. FORT HOWARD MD

(From the Department of Surgery, Veterans Administration Hospital)

INTESTINAL obstruction as a result of infestation with worms has occasionally been reported with *ascaris lumbricoides* usually the offending agent and with most of the cases occurring in children. The indictment of other worms as a cause of intestinal obstruction is rare. Many authors in their reviews of the problems involved in bowel obstruction do not mention *Enterobius vermicularis* as an etiologic agent.

*E. vermicularis* is usually and rightly regarded as a relatively innocuous inhabitant of the human intestinal tract producing as its main symptoms a pruritus ani and an occasional secondary infection of the perineum from scratching. The ova are ingested orally and are carried into the small intestine where copulation of the male and female occurs. The males succumb and the females with their ova migrate into the large intestine and out through the anus where the ova are deposited. A mild catarrhal inflammation of the intestinal mucosa produced by these worms has been reported by many authors. Manson-Bahr\* has found that mature worms may penetrate the mucosa, become encysted in the submucosa of the small intestine or appendix, and may give rise to inflammation in these areas.

Enervation of the adult female in the serosa of the sigmoid colon was found in the case being reported. A chronic intestinal obstruction secondary to inflammatory and fibrotic changes resulted. Such cases are infrequent in occurrence and interesting when their paucity is contrasted to the usually high rate of human infestation by this nematode within the United States.

### CASE REPORT

The patient was a 56-year-old white man, an elevator operator who was admitted to the hospital with complaints of diarrhea, hiccups and abdominal distention. He stated that the present illness had started about three weeks before admission with crampy, bloated pain and moderately severe diarrhea consisting of about eight stools a day. The stools were liquid in character and did not contain blood or purulent material. This episode of diarrhea lasted for about three days, and was followed by the intermittent passage of semisolid and liquid stool for the following 1½ weeks. The patient had liquid stool just prior to admission to the hospital. Periodic attacks of hiccups developed four days prior to admission and lasted as long as three days. When they became particularly persistent 8 days before entrance to the hospital he had a sudden severe attack of lower abdominal pain which lasted four hours.

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\*Manson-Bahr: Tropical Diseases, Baltimore, 1944, Williams & Wilkins Company.

at grade II in pyramidal abutment structure. Then a 100-ton roller was used to compact the material gradually developed but none of the existing one and present during this period except that on the 100-ton roller. The bottom 100-ton roller is now used.

A past history of gastritis, duodenal ulcer, severe diarrhea, and venereal infection are not listed. Large intestine procedures had not been performed previously. The patient had several other problems during World War II but otherwise had all procedures in the United States.

[illegible]

A most interesting group of the aboriginal Indians was the first mission on the hospital. A person named José María, of the II and large land, etc. were last found. He had been collected from the first of the mission, and was

[illegible][illegible][illegible]

Gradual progress was made in the development of the program. The program was designed to be a long-term project and was not intended to be a short-term project. The program was designed to be a long-term project and was not intended to be a short-term project. The program was designed to be a long-term project and was not intended to be a short-term project.

1) possibly due to the fact that the electron is not in the same state as it was before the interaction. The electron is not in the same state as it was before the interaction. The electron is not in the same state as it was before the interaction.





Improvement from this time on was quite rapid. Six weeks after the colostomy had been established, the patient was ready for further surgery.

Laparotomy was performed through an incision in the lower portion of the left rectus abdominis muscle. A firm mass about 6 cm. in length was present in the proximal portion of the sigmoid colon. A considerable number of adhesions were present in the area and portion of bowel immediately proximal to the lesion was moderately inflamed. Tumors were not palpable in the liver or in the remainder of the gastrointestinal tract. The character of the mass was such that it might be either an area of diverticulitis or carcinoma, although the diagnosis made at operation was diverticulitis. However with the realization of the fact that the surgeon is often subject to error during manual and visual examination of any mass.

The excision of the involved segment was done. The procedure of choice was extraperitoneal resection with immediate removal of the involved area of bowel. The proximal and distal ends of the mobilized bowel were peritonized, the mass was excised, and the fixed area of sigmoid removed. Convalescence from this operation was uneventful. About one month later the colostomy in the sigmoid colon was closed and three weeks following this operation the colostomy in the transverse colon was closed. The patient made a good recovery from both procedures.

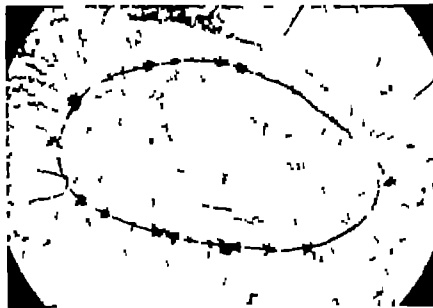


Fig. 1.—An adult female *E. coli* carcinoma in the wall of the sigmoid portion of the colon.

The pathologic examination showed grossly the specimen of colon segment of colon.

all defined, and fairly smooth. All small cysts was not separated in the manner characteristic of diverticula.

\*Reported through the courtesy of Dr. William B. Yandegraft.

Microscopic examination revealed the mucoid cyst to be entirely serosal in location and surrounded by granulation tissue or capsule of delicate connective tissues. Numerous plasma cells, polymorphonuclear neutrophilic leucocytes, and polymorphonuclear eosinophilic leucocytes were seen in the granulation tissue. Macrophages surrounded yellowish brown amorphous hyaline foreign bodies which appeared to be partially phagocytized. A delicate stroma of inflamed granulation tissue was present in the mucoid material. One of the cysts actually was an abscess, and in the purulent material parasite (Fig. ) was seen. Yellowish brown hyaline processes emanated from the surface of the parasite in the manner of subcutaneous. The wall of the parasite was formed from externally inward by cuticle layer of roughly rectangular cells, and a thin chitinous membrane. A thick layer of muscle lined the inner surface of the uterus seen in the center of the parasite but other structures were not found. The fistulous tract between the serosal cyst and the lumen of the bowel were lined with subacutely inflamed granulation tissue. The mucosa about the orifices of these tracts was chronically inflamed but elsewhere it was normal in appearance. A subcutaneous serosal inflammation opposite the cyst was present. Communication between the cyst and the peritoneal cavity were not found.

The parasitologist reported that the parasite found was *E. vermicularis*. Microscopically the microscopic section of the parasite possessed typical nematode characteristics such as an outer hyaline monolayer cuticle, subcuticular epithelium, and a layer of muscle cells. The particular part of parasite examined was cross section cut at the greatest width of the body just below the vulva of the adult female worm. The area was approximately 0.5 mm in diameter and contained part of distended uterus which did not hold ova. The distortum and absence of an ovary may be explainable through the mechanical destruction incident to unembedding and sectioning, through the degeneration caused by long enclosures in the cyst, or through possible natural sterility of the individual adult female nematode.

A number of stool examinations were done but findings in all were negative for parasites, blood and purulent material. Repeated differential leucocyte counts revealed normal number of polymorphonuclear eosinophilic leucocytes with the exception of one instance in which they were increased to 8 per cent.

When the final diagnosis was made by the pathologist a course of 1 per cent gentian violet was started. The drug was administered by mouth and also instilled into the distal limb of the colostomy in the transverse colon. A barium enema was given just before the final discharge of the patient from the hospital. Fluoroscopic and roentgenographic examination revealed slight filling defect at the site of closure in the transverse colon but the bowel was otherwise normal in all respects. The patient was asymptomatic at the time of discharge from the hospital.

The patient returned for examination about three months after the last operation. He stated that he felt quite well, had gained in weight and did not have symptoms referable to the large intestine. The abdominal wounds were well healed.

#### SUMMARY

A case report of a patient who had a chronic type of obstruction of the sigmoid colon owing to *E. vermicularis* is presented. After intensive preoperative preparation a staged procedure involving resection of the involved area of sigmoid colon was performed. The patient made a complete recovery. The incidence of this particular complication is unusually low in contrast to the reported high human infestation rate with *E. vermicularis*.

Improvement from this time on was quite rapid. Six weeks after the colostomy had been established, the patient was ready for further surgery.

Laparotomy was performed through an incision in the lower portion of the left rectus abdominis muscle. A firm mass about 6 cm. in length was present in the proximal portion of the sigmoid colon. A considerable number of adhesions were present in the rectum and the portion of bowel immediately proximal to the lesion was moderately inflamed. Tumors were not palpable in the liver or in the remainder of the gastrointestinal tract. The character of the mass was such that it might be either an abscess of diverticulitis or carcinoma, although the diagnosis made at operation was diverticulitis. However, with the realization of the fact that the surgeon is often subject to error during manual and visual examination of any mass, wide extirpation of the involved segment was done. The procedure of choice was extraperitoneal resection with incision of removal of the involved segment of bowel. The proximal and distal ends of the mobilized bowel were approximated, the mass was extirpated, and the affected area of sigmoid removed. Convalescence from this operation was unremarkable. About one month later the colostomy in the sigmoid colon was closed and about three weeks following this operation the colostomy in the transverse colon was closed. The patient made good recovery from both procedures.



FIG. 2.—An adult female *P. versicoloris* in the distal of the sigmoid portion of the colon.

The pathologic examination showed grossly the specimen segment of colon approximately 15 cm. in length with normal appearing mucosa but with roughened hemorrhagic

well defined, and fairly smooth. The characteristic of diverticular cysts was not separated in the manner characteristic of diverticular

Reported through the courtesy of Dr. William H. VanderGraft.

the diabetes, the remaining 3 having had ulcers when the diabetes was first discovered. The age distribution was unusual in that the onset of 13 of the 94 cases was after the age of 40 years. The symptoms were ordinarily vague with infrequent pain and hypoaecidity was present in only one of the cases of ulcer that developed after the onset of the diabetes. One factor which may be related to the infrequency of ulcer among diabetic patients is the relatively high incidence of anaemia that accompanies diabetes. Anaemia was found in from 70 to 40 per cent of diabetic patients, and the incidence increases with the greater length of duration of the disease.

Both the internal and external secretion of the pancreas may be implicated in ulcer formation. This study concerns certain aspects of the influence of the secretory activity of the pancreas upon the formation of ulcers induced by continuous histamine stimulation of the dog.

#### METHOD

Sixteen dogs were divided into Groups I, II, III, and IV, of four animals each. Group I served as controls, Group II was subjected to total pancreatectomy, Group III had partial duodenal ligation, and Group IV was made diabetic by the administration of insulin. All of these animals received regular intramuscular injections of histamine—beeswax using the technique of Hay, Vaseo, Cole, and Wingerlee. A large series of dogs which had been pancreatectomized 1 to 2 years prior to the beginning period on a dietary regime identical to ours was observed by Green and his workers at this institution and served as controls to demonstrate that ulcers do not develop spontaneously in these animals. Ligation of the pancreatic duct was performed in three other dogs which were used as additional animal controls for Group III. When they were sacrificed after 36 to 66 days, no ulcers had developed spontaneously. The milk and nutrient diet appeared to be adequate to protect against ulcer formation. Autopsy of all the dogs except a third of islet tissue indicated that complete ligation of the duct was obtained.

*Partial Pancreatectomy (Group II)*—Total extirpation of the pancreas was performed following a general technique outlined by Markwitz. Using aseptic technique and with the animal under general anesthesia an upper abdominal midline incision was made and the duodenum delivered out of the wound. The body of the pancreas was exposed by pulling the duodenum and jejunum up to the duodenum and elevating the pancreaticoduodenal vessels. Its separation from these structures must be done very carefully and was facilitated best as implied by gentle dissection with a No. 15 scalpel blade actually peeling the pancreas off the duodenum and jejunum around the pancreaticoduodenal vessels. The small pancreatic vessels were incised and hemostasis was secured by pressure. The main duct was ligated and sectioned but the accessory duct did not need to be isolated. The ligamentum pancreatocolic process for its insertion was readily removed by ligation of it separately blood supply and by ligating the mesentery. The tail was removed in a similar manner except that it had to be separated carefully from the splenic vessels and ligament. Insect in Omentum was wrapped around the duodenum to protect the raw surfaces. The abdominal wall was closed in layers.

## THE RELATION OF PANCREATIC SECRETION TO PEPTIC ULCER FORMATION

EFFECT OF PANCREATICTOMY, LIGATION OF PANCREATIC DUCTS AND DIABETES ON THE PRODUCTION OF HISTAMINE-INDUCED ULCERS IN THE DOG

FRANK J. POTH, M.D., F.R.C.P., F.R.C.S., J. MANROSE, JR., M.D., AND  
A. WILLIAM DELANCEY, M.D., GALVESTON, TEXAS

(From the *Special Research Laboratories, University of Texas Medical Branch*)

A RELATIONSHIP between pancreatic secretion and peptic ulcer formation has been long established. These observations have increased in importance with the development of a more definite picture of the effect of pancreatic disease on the pancreas and the subsequent influence upon secretory activity. Duodenal ulcers may be produced by the deviation of the alkaline secretion of the pancreas with external fistulas of the type described by Dugast, Montgery, and Ellis and Elman and H. Mann, by the internal duodenal fistula of Mann and Williamson, or by ligation of the pancreatic duct. These ulcers have usually been considered the result of mechanical deprivation of the duodenum of the neutralizing influence of the bile and pancreatic secretions on the acid effluent from the stomach. If however the duodenum is deprived of the alkaline secretions by pancreatic resection, duodenal ulceration rarely supervenes. The difference may be that whenever the pancreas is present and the external secretions are excluded from the bowels in immediate contact with the gastric secretions ulcers develop, while with simultaneous removal of the internal secretions by pancreatic resection ulcers do not develop when the external secretions are excluded because the blood sugar remains at a relatively high level with its stimulating influence of hypoglycemia on acid secretion by the glands of the stomach. Dugast reported the incidence of experimental peptic ulcers following external pancreatic fistulas as almost 100 per cent (over 100 cases) following ligation of the duct as 99 per cent (in 1 case) and following pancreatic resection as 13 per cent (300 cases). These figures correspond closely to the observations of other investigators. It may appear that in certain of these situations not adequately explained by failure of neutralization of the duodenum of the acid effluent of the stomach by the diverted alkaline secretions. The present series is apparent. Does the pancreas have an intrinsic effect upon ulcer formation other than that of mere alteration of the pH of the duodenal contents?

Certain statistical studies would tend to show that peptic ulcer develops infrequently in diabetic patients. In the largest series Wood reported 94 cases of ulcer in 1,000 diabetic patients, an incidence of 0.78 per cent. Of these however only 50 were known to have developed ulcers at the onset of

covered with a mattress suture of cotton through the capsule of the pancreas. The pancreas was completely separated from the duodenum and a bit of omentum was tied in place loosely between the pancreas and the duodenum. The post-operative care and feedings were the same as for the depancreatized animals, except that insulin was not needed.

*Alloxan Diabetic Group IV*—For the purpose of studying the effect of eliminating the action of insulin, a number of dogs were made diabetic by the administration of 75 mg of alloxan per kilogram of body weight. The degenerative changes on beta cells by the action of alloxan are not readily accomplished in dogs. By using the technique of withholding food for seventy-two hours as suggested by one of us (L. J. M.) four dogs were made diabetic as indicated in Table I. After stabilizing these animals on daily insulin therapy to maintain reasonable blood sugar levels on the tan larid milk and meat diet, insulin injection of histamine-in-wax was started.



Fig. 1.—Group I, Dog 11-1, Control. The animal was maintained on the standard meat and milk diet and received 4 mg of histamine-in-beeswax intramuscularly daily for forty-four days. The animal sacrificed and autopsied shows single duodenal ulcer as indicated. There had been no gross bleeding.

*Production of Ulcers*—The histamine-in-beeswax technique was used as described by Hay and associates. The ratio of ingredients used was 1 gm of histamine phosphate 0.5 cc of beeswax, and .9 cc of mineral oil which gives a mixture containing 100 mg of histamine base per cubic centimeter (1 gm of histamine phosphate is equivalent to 360 mg of histamine base). The histamine was ground to fine powder in a mortar which was kept warm over a water bath. Melted beeswax was added and thoroughly mixed with the powder then hot mineral oil was added and mixed until a perfectly smooth mixture was obtained. It was then sealed in rubber-stoppered 5 cc vial. The mixture solidified on cooling. For injection the vial was heated in a water bath and the mixture was aspirated into a syringe which had been warmed by rinsing it with

with continuous cotton sutures. Postoperatively careful management and replacement therapy maintained these animals in good condition indefinitely. Twelve hours after operation milk sweetened with corn syrup was given ad lib, and on the third day ground raw horse meat was added to the diet in increasing amount. About 15 gm of leuthin and 4 gm of pancreatin were mixed with the meat daily. Insulin administration was begun with 3 unit of regular insulin twelve hours postoperatively. The dosage was increased with the diet, and it was regulated by frequent blood sugar determinations. Two weeks after operation when the animal was taking full amounts of meat and milk, the insulin requirements were usually 6 to 8 units of protamine zinc insulin supplemented by 4 to 6 unit of regular insulin daily. Fasting blood sugar level ranging from 217 to 570 mg per cent indicated the completeness of the pancreatic extirpation. The histamine injections were not started until at least two weeks after the operation. During these injections the dogs received milk ad lib from 8 A M till noon and the meat ration at noon. No food was available between noon and 8 A M.

*Ligation of the Pancreatic Ducts, Group III*—Both pancreatic ducts were isolated out between cotton ligatures, and the pancreatic stump of the duct was

TABLE I

GROUP	ANIMAL NO.	AGE	DATE HISTAMINE ADMINISTRATION	WET WT. GRMS	INSULIN UNITS	REMARKS
I	5	10	44	0	0	Sacrificed, no ulcer present
	4	8	44	0	0	Sacrificed, one small duodenal ulcer (Fig. 1)
	11	8	15	0	0	Sacrificed, one small, superficial duodenal ulcer
	12	8	13	0	0	Sacrificed, one small ulcer pylorus
II	1	7	7	0	0	Died, numerous tears of duodenum and pylorus present
	2	15	6			Died, extreme ulceration of duodenum and pylorus and erosion of mucosa of esophagus (Fig. 3)
	5	14	4	+	0	Sacrificed, multiple duodenal ulcers, esophageal ulcers, extensive gastritis
	6	11	6		1	Sacrificed, 4 duodenal ulcers, hemorrhage from astrum of stomach
III	7	20			1	Died, extensive ulceration of duodenum and pylorus one ulcer in stomach 3 cm diameter (Fig. 3)
	8	20	4	+	0	Sacrificed, multiple duodenal ulcers ulcer in astrum of stomach
	9	10	6	+	1	Died, 4 duodenal ulcers
	10	9			1	Died, multiple duodenal ulcers
IV	A 8	9	12	0	0	Died, no ulceration present
	A 9	8.5	12	0	1	Died, one large perforated duodenal ulcer
	A 10	9.5	15	0	0	Died, no ulceration
	A 12	6	10	0	0	

Express four groups of animals in per kilogram of body weight daily of pancreas. Group III, ligation of both administration of alkali.

Summary of all lesions is given graphically in Fig. 4

This animal received only 100 mg of leucine-hydroxide daily

RESULTS

*Control Dog (Group I)*—There were four control animals, two of which were fed a dog biscuit diet, the other two receiving the standardized diet of meat and milk fed to all animals included in this study. The two animals on the routine dog biscuit diet developed typical single ulcers in the first part of the duodenum as shown in Fig. 1. The two dogs that were fed the standard meat and milk diet showed no signs of having developed ulcers. The one was skinned on the first fifth day. One of these dogs had a single small duodenal ulcer in the third part. Apparently the milk and meat diet prevented the formation of a ulcer in the animal and ameliorated the development of an ulcer in the other. This situation again emphasizes the intense reactions observed in the animals of Groups II and III. None of the control dogs had either gross bleeding or perforation.

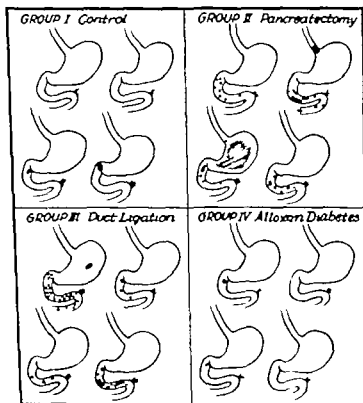


Fig. 1.—Stomach and duodenum of control dogs. The diagrams show the location of ulcers in the first part of the duodenum. The diagrams are not drawn to scale.

*Diabetic Dog (Group II)*—The result in the four pancreatized dogs were uniform and striking. Within four to seven days of first minimal incision, each of the dogs developed multiple severe ulceration of the duodenum. The least severe had four separate ulcers in duodenum and the most



hot mineral oil. A 1 cc Iu r f k syringe with a 20 g up needle found satisfactory for the injection. The injection was made intramuscularly at a single site into the back muscles. A dosage of 5 mg of histamine base per kilogram of body weight was administered daily in the late afternoon. The animals were sacrificed when they showed signs of having developed ulcers. On development of an ulcer the animal refused food, had occasional vomiting and bloody stools, and appeared ill.



the animal because of  
the ulcer which was  
the cause of its death

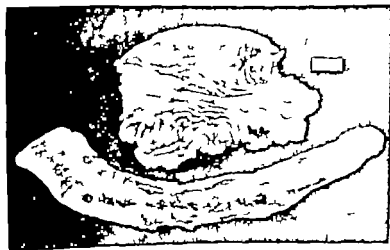


FIGURE III, Page 11- The ulcer was found on the back of the animal and was the cause of its death

RESULTS

*Control Dog (Group I)*—There were four control animals two of which were fed a dog biscuit diet the other two receiving the standardized diet of meat and milk fed to all animals included in this study. The two animals on the routine dog biscuit diet developed typical angle ulcers in the first part of the duodenum as shown in Fig. 1. The two dogs that were fed the standard meat and milk diet showed no signs of having developed ulcers. They were sacrificed on the fortieth day. One of these dogs had a single small duodenal ulcer the other had none. Apparently the milk and meat diet prevented the formation of an ulcer in the animal and ameliorated the development of an ulcer in the other. This protection against ulceration further emphasizes the intense reactions observed in the animals of Groups II and III. None of the control dogs had either gross bleeding or perforations.

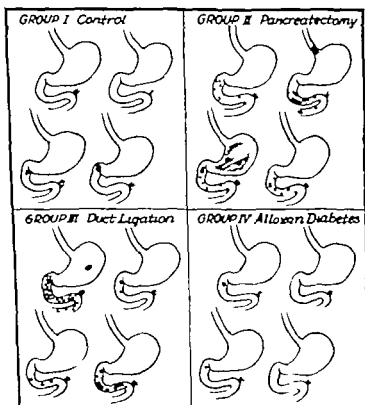


Fig. 1. Diagrams of stomachs and duodena of dogs in the four groups. The diagrams show the location of ulcers in the first part of the duodenum.

*Dogs of Group II*—The results of the experiment realized that dogs were uniform in their response to the administration of histamine and that the dogs developed multiple ulcers in the first part of the duodenum. The lesions were found to be separate ulcers in the duodenum and the most

severe had massive ulceration of the duodenum extending into the jejunum with two separate perforations, as well as erosion of the mucosa of the esophagus (Fig. 2). Of these four animals, two died, two had perforations, and bleeding occurred in all instances.

*Dogs With Ligated Pancreatic Ducts Group III*—The ulcers demonstrated by the group of dogs with ligated pancreatic ducts were even more severe than in the preceding group. One dog died in two days, after only two injections of histamine and showed massive confluent ulceration involving a large area of the duodenum with one large perforation, and also a 3 cm ulcer in the antrum of the stomach (Fig. 3). Two others died of perforations on the fifth and sixth days, and the fourth was sacrificed after four days. All showed multiple ulcerations, many of them confluent. Gross bleeding occurred in each instance.

*Dogs With Alloxan Diabetes Group IV*—None of the animals with alloxan diabetes showed signs of ulcer formation, although they were all ill probably due to the effect of the alloxan. All of these animals eventually died. A single duodenal ulcer was present in one of the four subjects.

The results observed in this experiment were essentially the same as in the control animals. If the diabetic state in any manner alters the tendency to histamine-induced ulcer formation, the difference is not sufficiently great to permit its demonstration by these studies.

#### DISCUSSION

Table I gives a summary of the results in each of the four groups. The comparison of the results in the control dogs with those in which the pancreatic secretion has been removed is striking. The two control animals which were placed on the same feeding regime as the dogs operated upon had no symptoms of ulcer and only one of them showed a ulcer after forty-six days. On the other hand, when the pancreatic secretion was diverted from the duodenum multiple severe ulcers developed in only seven days. In both the rapidity of development and of extent, these ulcerations were much more severe than have ever been observed in normal animals receiving histamine. It is obvious that the presence of the alkaline pancreatic juice in the duodenum is of great importance in the prevention of ulcers. Although removal of this secretion by extirpation of the gland does not of itself produce ulcers, it is apparent from the results of histamine stimulation that there is a strong predisposition to ulcer formation following pancreatectomy.

That diabetes exerts an inhibitory effect on the formation of peptic ulcers is not borne out by these experiments. The depancreatized animals were completely diabetic, yet they developed ulcers just as rapidly and just as extensively as did the animals that had only the pancreatic ducts ligated. And the alloxan diabetic animals showed no lesser tendency toward induced ulcer formation than did the normal controls.

A point of practical significance that can be derived from these experiments is the fact that removal of the pancreatic ligations of its ducts, frequently done in surgical procedures of the duodenum or pancreas, is not without some

danger of postoperative ulceration. It would seem to be advisable to reanastomose the pancreatic duct to the duodenum or jejunum whenever possible following resection of the head of the pancreas. Poth and Cattell<sup>14</sup> have described simple methods of accomplishing this procedure.

It is doubtful that resection of the vagus nerve at the level of the diaphragm should interrupt a sufficient number of the parasympathetic fibers to the pancreas to alter significantly its secretion.

# SUMMARY

A series of dogs are injected with histamine in beeswax after total pancreaticectomy after ligation of the pancreatic ducts, or after rendering the animals diabetic with alloxan and the tendency for peptic ulcer formation is observed. It is concluded that the presence of the neutralizing alkaline secretions per se is of importance in the prevention of ulcer formation and that these secretions should be returned to the proximal portions of the bowel to neutralize the acid effluent of the stomach whenever the normal relationship of pancreatic ducts and duodenum is destroyed.

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these compensatory mechanisms and their influence on the shape of the stomach is very difficult to evaluate at the present stage of knowledge owing to the great difficulty of investigating a seriously ill patient. In some cases scientific proof of the facts was obtained from x ray studies. Only further patient observation will clarify the position so that clinicians will be able to select suitable apparatus in a given set of conditions. It is to be hoped that it will be possible to indicate the type of tube which will be used on a given patient in order to avoid the delay caused by a wrong primary selection. A measurement of the intra abdominal pressure through the rectum prior to intubation, the assessment of the state of tension of the abdominal wall, the respiratory excursion as indicated by the change of abdominal pressure measured rectally on taking a deep breath and the height of the diaphragm in x ray plates are being considered.

The tentative indications which have so far emerged where difficulty may be expected in rapidly traversing the stomach are where the small bowel is distended and the skin of the abdomen is stretched taut or where the tonus of the abdominal wall, as in a young man of strong muscular build is maintained in spite of rapid distention of the small intestine. It seems probable that the small bowel only when distended influences the shape of the stomach. On the basis of three cases of primary large bowel obstruction with relatively little small bowel distention and in the presence of a greatly distended abdomen in which the skin was stretched taut no difficulty was experienced in traversing the stomach, although this was anticipated.

Thus, at present it is difficult to indicate a desirable line of approach with a given piece of apparatus except on the basis of trial and error with the reservations just mentioned. It is hoped that in time this problem may be clarified, either by the development of a universal tube or by a more exact knowledge of the condition obtaining in the abdomen.

#### TECHNIQUE

In order to use intubation in cases of moderate small intestinal distention where the stomach has previously been emptied by continuous gastric suction for some time or where the stomach is pressed upon by the distended bowel for any reason the technique of air injection into the stomach as suggested by Hamrick (1917) who claimed no rigidity has been found to be an extremely useful measure for rapidly traversing the stomach. Instead of using 500 cc. however I have found that 400 to 600 cc. are more successful since it is usually possible in these cases to get in a few inches of the tube into the fundus of the stomach. It is probable that the use of carbon dioxide or oxygen instead of air will be less likely to irritate the intension of the patient. So far in practice this comparatively small volume has not apparently resulted in deterioration of the patient. With this technique the air practice is pass the tube into the pharynx with the patient lying on his back, after which he is placed upright and positioned with the left. If his condition permits the legs are hung over the left side of the bed and he leans on a back rest during the swallowing of the tube. This avoids arrest of the tube at the lower end of the esophagus. After the first swallow the tube usually will descend rapidly to the stomach aided by gravity. If

well lubricated with a non-oily lubricant. The stomach is then inflated to 600 c.c. and the tube allowed to descend as far as it will go. The patient is then placed in the horizontal right-side-lying position and the intestinal balloon is tested for pyloric contractions. The object of this technique is to avoid arrest of the tube head in the fundus as rarely occurs where the stomach has a shelf known as a Cascade stomach due either to the stomach flopping over the transverse colon, or due to an elevation in the posterior gastric wall caused by the pancreas. These are the only causes of arrest in the fundus of the stomach which have been discovered so far apart from the condition of the stomach found in the severest degrees of small bowel distention.

The problem of intubating the severest degrees of distention has occupied the attention of clinicians almost since the introduction to surgery of intestinal intubation by Abbott and Jobert in (1938). It is these cases which offer the most anxiety with the result that the best method of treatment is still in doubt. Surgeons generally dislike operating upon patients with great distention, and if an intestinal tube could be rapidly introduced into the duodenum so that more consistent and earlier decompression in these cases could be achieved, the mortality from uncomplicated bowel distention might be considerably reduced. During a period of one year some ten cases were encountered in which neither air injection with manipulation under fluoroscopy nor waiting for periods of twelve hours for advancement of the tube head into the duodenum has altered the position of the head of the tube. The tendency in these cases has been for the tube to lie just under the diaphragm on the left side. It gradually became apparent, as data accumulated from the use of small quantities of watery barium sulfate that the fundamental difficulty in intubating these most severe cases of distention is the circumstance that the stomach wall has become pressed together by the distended bowel against the liver to such an extent that air injection will no longer distend the stomach sufficiently to permit passage of the tube (Fig. 1). Distention twisting kinking and abnormal position of the first and second part of the duodenum has not been found. The limited number of cases (six) in which I have used intubation successfully so far.

There is moreover in addition to the problem of accelerating transit of the tube from the stomach to the duodenum, the problem of rather frequent arrest of the tube either in the retroperitoneal duodenum or in the upper reaches of the jejunum beyond the duodeno-jejunal suspensory ligament. This circumstance is one that interferes seriously with early decompression of the distended intestine. Until this problem is resolved by agents which will permit more consistent early decompression of the distended segments of obstructed intestine conservative decompression will not have achieved its maximal usefulness. This aspect of the problem is being carefully studied in this laboratory.

Upon recognition of the condition of the stomach in severe cases of distention, a simple method for overcoming the difficulty was devised. The work of Hemmeter (1906) at the Johns Hopkins Hospital suggested that a gastric balloon might be used. Hemmeter was carrying out kymographic studies on the human intestine and he noticed that frequently the balloons were arrested





well lubricated with a non-oily lubricant. The stomach is then inflated to 600 c.c. and the tube allowed to descend as far as it will go. The patient is then placed in the horizontal right-side-lying position and the intestinal balloon is tested for pyloric contractions. The object of this technique is to avoid arrest of the tube head in the fundus as rarely occurs where the stomach has a shelf known as a Cascade stomach due, it is thought, to the stomach's flopping over the transverse colon or duodenum to an elevation in the posterior gastric wall caused by the pancreas. These are the only causes of arrest in the fundus of the stomach which have been discovered so far apart from the condition of the stomach found in the severest degrees of small bowel distention.

The problem of intubating the severest degrees of distention has occupied the attention of clinicians almost since the introduction to surgery of intestinal intubation by Abbott and Johnston (1938). It is these cases which offer the most anxiety with the result that the best method of treatment is still in doubt. Surgeons generally like to operate upon patients with great distention and if an intestinal tube could be rapidly introduced into the duodenum so that more consistent and earlier decompression in these cases could be achieved, the mortality from uncomplicated bowel distention might be considerably reduced. During a period of one year some ten cases were encountered in which neither air injection with manipulation under fluoroscopy nor waiting for periods of twelve hours for advancement of the tube head into the duodenum has altered the position of the head of the tube. The tendency in these cases has been for the tube to lie just under the diaphragm on the left side. It gradually became apparent, as data accumulated from the use of small quantities of watery barium sulfate, that the fundamental difficulty in intubating these most severe cases of distention is the circumstance that the stomach walls have become pressed together by the distended bowel against the liver to such an extent that an injection will no longer distend the stomach sufficiently to permit passage of the tube (Fig. 1). Distortion, twisting, kinking, and abnormal position of the first and second part of the duodenum have not been found in the limited number of cases (six) in which I have used intubation successfully so far.

There is, moreover, in addition to the problem of accelerating transit of the tube from the stomach into the duodenum, the problem of rather frequent arrest of the tube either in the retroperitoneal duodenum or in the upper reaches of the jejunum beyond the duodenojejunal suspensory ligament. This circumstance is one that interferes seriously with early decompression of the distended intestine. Until this problem is resolved by a agent which will permit more consistent early decompression of the distended segments of obstructed intestine conservative decompression will not have achieved its maximal usefulness. This aspect of the problem is being carefully studied in the laboratory.

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a possible without coiling inflation of the gastric balloon is commenced by displacement of air by siphonage of water from one gallon bottle to another (Fig 3). The patient should be lying on the right side feet down preferably to about 90 degrees or more. An inflation proceeds, more and more of the tube swallowed with the sipping of water until the patient complains of great discomfort. The air of course becomes heated to body temperature and expands, and upon removal in the air will seemingly be removed than was put in. The maximum inflation that the patient can stand is used and maintained for only a short time. A man has 1700 cc. of air have been used. Usually 1500 cc. are sufficient. Once the head of the tube has been delivered into the pyloric region the gastric balloon is completely inflated and the patient returns to the ward and is placed in the most favorable position for advancement of the tube. Sometimes 5 cc. of air are put into the intestinal balloon, or into the inflatable gravity director head if this is used in place of the intestinal balloon.

Such is then the method to late of using the experimental gastric balloon apparatus. Two of the early cases are described here.

#### CASE REPORTS

CASE 1.—A emaciated white man, aged 40 years. Discharged from another hospital in high nervous state. The diagnosis of liver colic of six months duration.

Intubation as used in the first instance in order to try to improve his chronic condition prior to operation since he had low grade intermittent obstruction. The small intestine at this time not greatly distended.

On August the patient started for the physician found necessary to give 4 gr. of sodium nitrate every period of three hours in order to give him cooperation. Once the tube had been introduced to the over the duodenum intubated in matter of minutes, as evidenced by the radiograph. The patient immediately pulled the tube out and it replaced at the duodenum. It was eight hours later the tube found to be well down the gut and decompression achieved.

The tube remained in place until ten days later at which time found to be severe. The skin of the abdomen stretched tight and the abdominal wall offered considerable resistance to the palpating fingers. A Miller Abbott tube was inserted with great direct head inserted to the help of the patient his time but it found impossible to get the tube to advance by pushing into the nostril after it just entered the stomach, above the mark on the tube. A radiograph at this point showed the gastric director head just below the diaphragm and in the fundus of the stomach, hanging to the left of the vertebral column. Ejection of air into the stomach did not distend the fundus significantly. A tube with gastric balloons improved and inserted into the stomach. After the gastric balloons filled the gravity director head found to be to the right of the vertebral column in the pylorus. Fig 4.

At this point the patient became uncooperative and pulled the tube back to the level of the right nostril. The use of the pressure of the pressure of the stomach (swallowing) to break the neck of the gastric balloon again intubated and the tube delivered to the pylorus. However by this time it decided to operate since the possibility of strangulation of the bowel could not be excluded. At operation the low lying fundus of the stomach of blood supply due to its position around the duodenum. A proper decompression with a gastric balloon decompression carried out.

Twenty-four hours later the patient had recovered from the operation, the intubation had been back had been left in the stomach. proved to be fairly well recovered.

into the duodenum. He suggested from his observations that it might be possible to construct a balloon with a magenstrasse or guiding trough which could be introduced into the normal stomach so that subsequently tube could be guided down the magenstrasse into the duodenum. It seemed that this scheme would be impracticable for this particular application, since after introducing and inflating a balloon in the stomach in severe cases of distention, conditions will be no more favorable for subsequent passage of a tube than before. It was decided to attach the balloon near the distal end of the tube. This was done and an experimental tube was assembled (Fig. 3). It was thought probable that if this balloon were to be partially introduced into the gas bubble which seems always to be trapped in the fundus of the stomach in

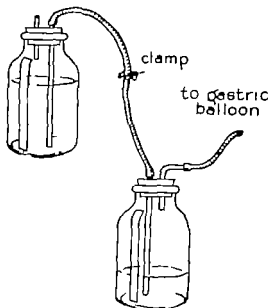


Fig. 3.—The method of inflation in the initial cases in which the gastric balloon was used. The elevated bottle is raised four feet above the lower bottle.

these cases, and inflated the walls of the stomach would be forced past and thus the tip of the tube would be carried to the pylorus. This scheme has been found to work satisfactorily in the limited number of cases so far attempted. In the event that it should be desired to try out this piece of apparatus, I would urge that the details of construction be followed exactly. Many difficulties will thereby be avoided. Further development is in progress. It will be noticed that there are no aspiration holes in the apparatus proximal to the balloon. This is very important, since it may be impossible to get more than the tip of the tube into the fundus of the stomach. Thus, it may be impossible to flat the fundus somewhat in attempting to get the gastric balloon as far as possible into the stomach. Fluoroscopic visualization has been used regularly on these cases. After getting much of the gastric balloon into the stomach

of the gastric balloon in matter of minutes. The abdomen following asphytic decompression was now full but not tightly stretched as before. Fifteen hours later the bowel was found to be decompressed and the tube still down the gut.

The following day the patient died. Autopsy revealed multiple long ulcers.

The points brought out by this case were that a tube could easily be passed into the duodenum of this patient in the absence of distention of the abdomen and that it was possible to get the same tube into the fundus of the stomach in the presence of severe distention—that by using the gastric balloon it was possible to deliver the end of the tube to the pylorus—that after decompression peritively when the abdomen was again soft it was again possible easily and quickly to pass the tube into the duodenum.

This case gave the opportunity to study the gastric balloon and much valuable time to the patient had to be wasted in discerning what was required. It was unavoidable that the patient had to be taken to surgery owing to prolonged attempts at intubation. It served to show the difficulty of studying these cases scientifically. Nevertheless much valuable information was gained for use in subsequent cases.

C.—A young Irish man, aged 18 years, admitted with ten days history of complete obstruction. For days prior to admission he gave a history of the dyspepsia, not severe. The report of the investigation revealed that the stomach showed most peculiar abnormality: the small loop which is not out of shape. The duodenum is highly dilated, the possibly partial contraction of the lower end of the duodenum not total. It was passed on into the small intestine.

On admission the abdomen moderately distended and tender. The good tone of the abdominal musculature. A year of appendicitis was reported as the previous history. The report of the barium meal and in view of the condition of the abdomen, it was decided to use a gastric balloon. The back radiograph after passage of the tube into the fundus of the stomach showed the gravity directed head lying under the diaphragm to the left of the vertebral column. The axis of the body of the stomach were outlined by a streak of residual barium lying in position transversely to the level of the joint between the tenth and eleventh thoracic vertebrae. A distended loop of jejunum was visualized below the Under fluoroscopic visualization 50% of very barium sulfate were swallowed. This filled the fundus of the stomach and remained in position and did not move across the right of the vertebral column even with manipulation and change of position.

The stomach was then inflated with air in position down the stomach lumen until eructation occurred after every attempt. The tube was then distended the fundus somewhat but it gave no effect on the position of the gravity director head. After a few minutes the patient was tilted 45 degrees feet down on the right side and the gastric balloon inflated to two-thirds distension. The gravity head was then moved down. More than the patient and further down the gravity head was moved. There was some doubt as to the position of the gravity head at this stage (Fig. 3) as 50% of very barium sulfate were injected down the tube. This barium passed immediately on to the lower.

Since the patient had been in the position of the barium meal for some time he was tilted 50% of very barium sulfate in order to secure the fundus. At this time the small loop of the duodenum had expanded and the patient was returned to the ward, was better and thirty minutes after passage of the tube to the nose. The patient placed in a high position over the head of the bed and the balloon partially inflated and he



Fig. 1 (a) — This shows the same as shown in Fig. 1 (b) but with the air. The air is directed in the left lateral balloon is shown, carried to the right of the vertebral column. The loops of the left and right bow are being forced down by inflation of the stomach.



over all over both bones. The intra-  
the gastric. Bone.  
The introduction of the tube into the  
stomach with the intestinal balloon per-  
forms the. The very bottom and  
walls of the stomach can be seen in  
of the dissection.  
The same was carried on several days.

before dissection and before dissection.

of the gastric balloon in about 15 minutes. The abdomen following aseptic decompression was now full but not tightly stretched as before. Fifteen hours later the balloon was found to be decompressed and the tube fell down the gut.

The following day the patient died. A autopsy revealed multiple lung abscesses.

The points brought out by this case were that a tube could easily be passed into the duodenum of this patient in the absence of distention of the abdomen and that it was possible to get the same tube into the fundus of the stomach in the presence of severe distention—that by using the gastric balloon it was possible to deliver the end of the tube to the pylorus—that after decompression operatively when the abdomen was again soft it was again possible easily and quickly to pass the tube into the duodenum.

This case gave the opportunity to study the gastric balloon and much valuable time to the patient had to be wasted in discerning what was required. It was unavoidable that the patient had to be taken to surgery owing to prolonged attempt at intubation. It served to show the difficulty of studying these cases scientifically. Nevertheless much valuable information was gained for use in subsequent cases.

Case 2.—A young Chinese man, aged 16 years, admitted with tendency to try for complete abstinence. For the past 12 months he has been suffering from the loss of weight and loss of appetite. The report of his digestion revealed that the stomach seemed most peculiarly large for the small bowel which went out of shape. The duodenum slightly dilated, the possible partial obstruction of the lower end of the duodenum, not too large, passed on into the small intestine.

On admission the abdomen moderately distended and tender with good tone of the abdominal muscles. A scar from an appendectomy ten years previously was prominent. I was of the report of the barium meal and in view of the condition of the abdomen, it decided to use the gastric balloon. The erect radiograph after passage of the tube into the fundus of the stomach showed the gastric director head lying under the diaphragm to the left of the vertebral column. The walls of the body of the stomach were visualized by the contrast of the barium lying in position transverse to the level of the point between the tenth and eleventh thoracic vertebrae. A distended loop of jejunum visualized below this. Under fluoroscopic examination all of the barium was swallowed. This filled the fundus of the stomach and remained in the stomach and did not move across to the right of the vertebral column even when the patient was changed from position.

The stomach then inflated with air in position down to the lower umbilicus until erect film secured. Every 30 seconds the tube was inserted into the fundus somewhat but it kept on the position of the gastric director head. After 15 minutes of various changes of position. The patient tilted 45 degrees feet down on the right side and the gastric balloon inflated to about 40 cm. The gastric fundus was seen to move down. More air passed and further advance of the gastric head was observed. There was no more doubt of the position of the gastric head. It was stage 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100.

When the patient had about 100 cc of air in the stomach he was moved to the right side and the gastric balloon inflated to about 40 cm. The gastric fundus was seen to move down. More air passed and further advance of the gastric head was observed. There was no more doubt of the position of the gastric head. It was stage 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100.



Fig. 1 (Case 1) — This shows the diaphragm heart like the balloon 1 balloon is shown carried the right of the vertebral column. The loops of distended small bowel are seen to true second row the left side of the stomach.



Fig. 2 (Case 1) — This shows the radiograph taken one hour after the first X-ray. The diaphragm heart is seen to be more or less in position with the gastric bubble.

Fig. 3 (Case 1) — This shows the radiograph taken one hour after the first X-ray. The diaphragm heart is seen to be more or less in position with the gastric bubble.

of the gastric balloon in matter of minutes. The balloon following aseptic decompression was now full but not tightly stretched. Before fifteen hours later the boy found it he decompressed and then he did down the gut.

The following day the patient died. A autopsy revealed multiple long abscesses.

The points brought out by this case were that a tube could easily be passed into the duodenum of this patient in the absence of distention of the abdomen and that it was possible to get the same tube into the fundus of the stomach in the presence of severe distention. That by using the gastric balloon it was possible to deliver the end of the tube to the pylorus. That after decompression peratively when the abdomen was again soft it was again possible easily and quickly to pass the tube into the duodenum.

This case gave the opportunity to study the gastric balloon and much valuable time to the patient had to be wasted in discerning what was required. It was unavoidable that the patient had to be taken to surgery owing to prolonged attempts at intubation. It served to show the difficulty of studying these cases scientifically. Nevertheless much valuable information was gained for use in subsequent cases.

CASE 4.—A young boy, aged 16 years, admitted with ten-day history of complete obstruction of the small intestine. He was given a lumbar puncture and the fluid was clear. The report of this examination revealed that the stomach contained about 100 cc. of fluid in the small bowel which was not out of the peritoneum. The duodenum was slightly dilated, the possible partial obstruction of the lower end of the duodenum, not yet fully ascertained as to the small bowel.

On admission the abdomen was moderately distended and tense. The condition of the abdominal musculature was from peritonitis. The patient was given a gastric balloon. The report of this examination revealed that the stomach contained about 100 cc. of fluid in the small bowel which was not out of the peritoneum. The duodenum was slightly dilated, the possible partial obstruction of the lower end of the duodenum, not yet fully ascertained as to the small bowel.

The stomach was then inflated with air. The patient was given a gastric balloon. The report of this examination revealed that the stomach contained about 100 cc. of fluid in the small bowel which was not out of the peritoneum. The duodenum was slightly dilated, the possible partial obstruction of the lower end of the duodenum, not yet fully ascertained as to the small bowel.

When the patient had died the boy was given a gastric balloon. The report of this examination revealed that the stomach contained about 100 cc. of fluid in the small bowel which was not out of the peritoneum. The duodenum was slightly dilated, the possible partial obstruction of the lower end of the duodenum, not yet fully ascertained as to the small bowel.



gastric balloon completely deflated. During the night 1400 cc of drainage occurred and radiograph (Fig. 6) taken fifteen hours after introduction of the tube showed the tube in the second part of the duodenum, with the barium at 11 in the fundus of the stomach.

The intestinal balloon inflated 1 lb and the patient allowed to remain on his left side for 24 hours. A radiograph taken 24 hours after introduction of the tube and after 4000 cc. of intestinal fluid had been removed showed the barium depot in the fundus to have thinned and passed into the gut. The gut was almost decompressed. A further radiograph forty-eight hours after introduction of the tube showed the gut completely decompressed and the end of the tube coiled in the pelvis with an incarcerated mass of small bowel. This was confirmed by fluoroscope examination with injection of water barium down the suction lumen of the tube after sealing the lower presumably with the intestinal balloon inflated for short time to each degree to extend the bowel.

The patient then prepared for operation and put on liquid diet. Nine days after duodenostomy he was operated upon, good results since red section took place, however section was discontinued. No improvement of blood supply of the gut was found and enterotomy was performed and the tube pulled back just proximal to the site of the operation. Back was the last four or five feet of the ileum.

On the fourth postoperative day the bowels moved, the tube removed and the patient made an uneventful recovery.

#### SUMMARY

As a result of studying some 900 cases of small bowel distention in which tubes fitted with thin-walled rubber sack partially filled with mercury and attached terminally were used, the stomach was found to be an important factor in bringing about rapid intubation of the bowel. Techniques for a rapid delay due to the state of the stomach are described, including the use of the gastric balloon developed to fit the part of the wall of the stomach in cases where gas in jection into the stomach will not dilate the stomach sufficiently to permit passage of the tube.

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# EXPERIMENTAL STUDIES IN VASCULAR REPAIR

## I. COMPARISON OF RELIABILITY OF VARIOUS METHODS OF END-TO-END ARTERIAL SUTURES

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THE technique of vascular repair has assumed increased importance with the advent of vascular shunt operations in such conditions as congenital heart disease associated with reduced pulmonary blood flow and portal hypertension. The introduction of methods of excising and repairing the coarcted aorta,<sup>1,2</sup> or of by-passing it with a subclavian-aortal anastomosis, and with recent emphasis upon the advantages of maintaining or restoring the continuity of the artery in the surgery of aneurysms and arteriovenous fistulas. Numerous methods of anastomosing and repairing blood vessels have been tried in the past with varying results. Some of these methods have been abandoned while others have continued to be used. In operating for pulmonary stenosis or atresia Blalock used the continuous everting mattress suture introduced by Clermont<sup>3</sup> and Dorrance while Potts, Smith and Gibson employed the continuous over and over suture of Carrel. In cases of coarctation of the aorta, Gross used the continuous mattress and Crafoord and Whin the continuous plain suture. Crafoord also used sutures which do not penetrate the intimal layer a principle advocated by Jassinowsky. In the repair and anastomosis of peripheral arteries Freeman recently used the Carrel suture and Shumacker the interrupted everting mattress technique of Jaboulay and Brian.

The literature contains numerous studies which reveal the incidence of successful result and of complication with various techniques in the hands of different investigators. The result obtained with any given method varies considerably. It is apparent that the relative worth of the various techniques can be determined best by controlled experiments performed upon one selected artery in one species of animal by the same group of workers. In this report we wish to present such an effort directed toward inquiring into the comparative reliability of four types of end-to-end repair: interrupted plain, continuous plain, continuous mattress, and interrupted everting mattress sutures.

We have selected these four types of suture for comparison because they represent the animal principles of suture methods which have proved most trustworthy. The techniques of plain interrupted through-and-through sutures and of continuous over-and-over sutures embody the accurate end-to-end approximation of the artery wall the exposed ends of the vessel being maintained in an everted position during the operation by traction sutures. The mattress techniques exemplify those methods which aim at approximation of the artery wall with the intima fixed in an everted position. Continuous and interrupted sutures of both types were selected for study because there are certain theoretical

gastric balloon completely deflated. During the night 1400 cc of drainage occurred and radiograph (Fig. 6) taken fifteen hours after introduction of the tube showed the tube in the second part of the duodenum, with the barium at 11 in the fundus of the stomach.

The intestinal balloon inflated fully and the patient allowed to remain on his left side for ten hours. A radiograph taken twenty-five hours after introduction of the tube and after 4000 cc of intestinal fluid had been removed showed the barium depot in the fundus to be thinned and passed into the gut. The gut was almost decompressed. A further radiograph forty-eight hours after introduction of the tube showed the gut completely decompressed and the end of the tube coiled in the pelvis with an incarcerated mass of small bowel. This was confirmed by fluoroscopic examination. On injection of water barium down the suction lumen of the tube after sealing the bowel proximally with the intestinal balloon inflated for short time to such degree that it distended the bowel.

The patient was then prepared for operation and put on liquid diet. Nine days after drainage he operated upon, good condition, no re-distention took place whenever suction was discontinued. No impairment of blood supply of the gut was found and enterolysis as performed and the tube pulled back just proximal to the site of the operation back as the last four or five feet of the ileum.

On the fourth postoperative day the bowel moved, the tube removed, and the patient made an uneventful recovery.

#### SUMMARY

A result of studying some 200 cases of small bowel distention in which tubes fitted with thin walled rubber neck partially filled with mercury and attached terminal were used the stomach was found to be an important factor in bringing about rapid tubation of the bowel. Techniques for avoiding delay due to the state of the stomach are described, including the use of the gastric balloon developed to force apart the wall of the stomach in cases where gas injection into the stomach will not dilate the lumen sufficiently to permit passage of the tube.

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plain sutures were an over-and-over continuation of such a suture. The interrupted mattress sutures were horizontal. If sutures the continuous mattress sutures were a continuation of this same horizontal mattress technique. The continuous sutures were tied to each of the guide sutures, care being taken not to constrict the lumen by drawing the suture too tightly. The interrupted sutures were placed approximately one millimeter apart the continuous sutures a little closer. The sutures were passed through the vessel wall as near the cut edge as was practical, generally a distance of about twice the diameter of the needle as advised by Deeders.<sup>20</sup> Upon completion of the anastomosis the distal and then the proximal, clamp was removed and gentle pressure was maintained over the suture line until there was no bleeding. Occasionally it was necessary to use an additional suture in order to achieve hemostasis. The fascia was closed with interrupted silk sutures and the skin with subcuticular or cutaneous sutures of silk. In each animal both carotid arteries were divided and sutured except in occasional animal in which one carotid was excised for histologic or other study. A different method of suture was ordinarily used for each of the two vessels and, in general the four types of suture were employed in rotation throughout the study. No anticoagulants and no antibiotics or chemotherapeutic agents were used.

Specimens were excised at varying intervals and examined carefully for leakage, intima, thrombosis, aneurysm, and other complications.

#### RESULTS

Ninety-six sutured arteries were examined at intervals of from four to seven-six days after operation (average twenty three days). In Table I data are recorded which give the results with the four different types of suture. It would appear that the mattress techniques gave better results than were obtained with the use of plain sutures, and that interrupted sutures proved somewhat more reliable than continuous sutures. Of twenty three arteries repaired by the Carrel method six were thrombosed, in one there was a tiny aneurysm, and in three there were strictures, in one of which a partial dehiscence had occurred. Altogether there were complication in ten, or 43 per cent, and in thirteen healing had occurred without complication (56 per cent). Of twenty two arteries repaired with interrupted plain sutures, one was occluded by thrombosis, another was strictured and thrombosed, three others had strictures, one had a small aneurysm, and two had a dehiscence. Complications were present in eight, or 36.4 per cent while fifteen or 68.6 per cent healed without mishap. Of twenty seven arteries repaired with continuous mattress sutures, four were thrombosed, one was thrombosed and strictured, one had a very small aneurysm and another had a dehiscence. Complications were present in seven (25.9 per cent) and twenty (74.1 per cent) healed without complications. Of twenty four arteries anastomosed with interrupted mattress sutures, three were thrombosed, one thrombosed and strictured, and another had a stricture. Altogether there were complication in five or 20.8 per cent and no complications in nineteen, or 79.2 per cent. Sixty per cent of the forty five arteries repaired with plain suture and 61 per cent of the fifty-one repaired with mattress sutures healed without complications.

advantages and disadvantages of each. Various other methods of repair not included in this investigation are in reality variants of those we have employed.

We have not undertaken to study suture methods which omit penetration of the suture through the intimal layer such as were originally advocated by Jassinowsky and Briel. They were largely abandoned after the work of Silberberg, Napalkow, and Dorfl.<sup>10</sup> Though Crafoord has used this principle with great success in suture of anastomosis, it is a method which is technically impractical in suturing small arteries and is possible in suturing veins. We have also omitted from consideration nonsuture techniques such as those of Payr,<sup>11</sup> Lespinasse, Fisher, and Eisenstaedt,<sup>12</sup> and Blakemore, Lord, and Steffen.<sup>13</sup> Though such methods undoubtedly have some applicability in certain unusual circumstances and in situations in which vascular repair must be attempted by surgeons untrained in suture techniques, they are not a generally applicable and have certain disadvantages. In subjecting the suture and nonsuture methods to the critical test of anastomosis in anastomosis, I have found the suture method more reliable.

#### MATERIAL AND METHODS

Mongrel dogs, varying in weight from 4 to 44 kilograms were used. Operations were performed under nembutal anesthesia, using aseptic technique. The common carotid arteries were exposed through a transverse anterior incision in the neck. As soon as the vessel was isolated its diameter was carefully measured and recorded. A segment of the artery was then carefully stripped of adventitia. After applying rubber-rod wireline clamps proximally and distally the vessel was cut transversely with small sharp scissors through a little more than half its circumference. The mid portions of the cut end were then brought together with the first guinea traction suture. This first suture was placed before the vessel was completely transected because it saved time and effort in holding rotation of one segment of the artery upon the other. The artery was next divided completely and the remaining traction sutures were placed and tied. In the case of small arteries three of these guide sutures were inserted equidistantly from one another according to the suggestion of Crile.<sup>14</sup> In the case of larger arteries four were used according to the suggestion of Fournier.<sup>15</sup> All blood was washed from the lumen of the artery with saline solution and the vessel and surrounding tissues were kept moistened throughout the procedure. Deknatel silk, 000000, and round catgut needles, N 14 were used sutured and needles were kept lubricated with mineral oil. Care was taken to avoid pinching or otherwise traumatizing the artery.

Traction upon three or four guide sutures triangulated and approximated the approximate vessel, opposed the cut end in position for anastomosis, and permitted rotation so as to expose successively the segments of the triangular aperture. One segment at a time was sutured. The interrupted plain sutures were simple sutures passed through the entire thickness of the artery from without into the lumen of one segment and then out through the other segment. The continuous

(This report subject to editing is based on the material as received from the authors. The careful removal of the lower external arterial is obvious to the reviewer. It is completely removed.)

In analyzing the result of this study it is important to make certain that the outcome in the various groups was dependent upon the type of suture used and not upon some other variable. Except for the difference in the suture technique most of those factors which might conceivably influence the result were constant. The same artery was used, the same general operative technique, the same operators, and the needles, suture materials, and clamps were identical. Two factors, however, require analysis—the length of time between the arterial repair and the examination of the specimen and the size of the sutured artery. The first might be of some significance for although such complications as dehiscence and thrombosis undoubtedly occur early, others, such as strictures or aneurysms, might not be evident for some time after the procedure has been accomplished. The second is undoubtedly the most important variable which might influence the result.

In Table II data are listed concerning the interval of time which elapsed between the operative procedure and examination of the specimen. It will be seen that the duration of the anastomoses did not vary greatly in the different groups. The percentage of specimens examined in ten days or less, in from eleven to thirty days, and after thirty days or more was almost precisely the same in the groups repaired by continuous and interrupted plain and continuous mattress sutures. A slightly smaller percentage of those repaired by interrupted

TABLE II. DURATION OF ANASTOMOSES. TIME OF EXAMINATION.

TYPE OF SUTURE	PLAIN			MATTRESS		
	TEN OR LESS	FROM ELEVEN TO THIRTY DAYS	AFTER THIRTY DAYS OR MORE	CONTINUOUS	INTER- RUPTED	ALL
Number of arteries sutured	1	2	43	4	1	31
Number examined in 10 days or less	9 (90%)	8 (40%)	1 (2%)	10 (25%)	8 (80%)	14 (45%)
Number examined in from 11 to 30 days	9 (90%)	9 (45%)	1 (2%)	10 (25%)	1 (100%)	11 (35%)
Number examined 30 days or more after operation	8 (80%)	5 (25%)	11 (26%)	7 (25%)	4 (40%)	11 (35%)
Average duration of anastomosis in time of exami- nation in days	7.5	22	4	4	19	22

mattress technique were examined in ten days or less and after thirty days or more and a correspondingly larger percentage in from eleven to thirty days. Of the fifteen arteries repaired with plain sutures, 33 per cent were examined in ten days or less, 33 per cent in from eleven to thirty days, and 34 per cent after thirty days or more. In the case of the fifteen arteries anastomosed by mattress sutures these percentages were almost the same—33, 43, and 22 per cent respectively.

In Table III the data are given concerning the size of the arteries sutured. Very small arteries were used in only 30 per cent of those repaired with plain sutures, and in one-third of those repaired with mattress sutures. Since it is apparent that the chance of success is greater with larger vessels, it is clear that

TABLE 1. COMPARISON OF RESULTS OF E. TO E. JERUSALEM, 1960, AND IN THE 1961 TO 1962

No. of sites	MAIN			4 sites		
	NUMBER	PERCENT	ALL	NUMBER	PERCENT	TOTAL
Number of sites on red	21	100	48	27	100	90
Number of sites on red	0	0	5	5	4	17
Number with structure	1	41	7	11	36	10
Number with structure	1	1	3	1	0	3
Number with structure	11	52	3	1	0	4
Number with structure	10 (47.6%)	4 (20.4%)	1 (4.8%)	7 (25.9%)	5 (20.4%)	20 (41.0%)
Number without any trees	11 (52.4%)	11 (52.4%)	27 (56.8%)	20 (74.1%)	18 (70.0%)	68 (69.5%)

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Three marked under structure.

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This case is also listed under structure.

In analyzing the results of this study it is important to make certain that the outcome in the various groups was dependent upon the type of suture used and not upon some other variable. Except for the difference in the suture technique, most of those factors which might conceivably influence the result were constant. The same artery was used, the same general operative technique, the same operators, and the needles, suture materials, and clamps were identical. Two factors, however, require analysis: the length of time between the arterial repair and the examination of the specimen, and the size of the sutured artery. The first might be of some significance for although such complications as dehiscence and thrombosis undoubtedly occur early, others, such as strictures or aneurysm, might not be evident for some time after the procedure has been accomplished. The second is undoubtedly the most important variable which might influence the result.

In Table II data are listed concerning the interval of time which elapsed between the operative procedure and examination of the specimen. It will be seen that the duration of the anastomoses did not vary greatly in the different groups. The percentage of specimens examined in ten days or less, in from eleven to thirty days, and after thirty days or more was almost precisely the same in the groups repaired by continuous and interrupted plain and continuous mattress sutures. A slightly smaller percentage of those repaired by interrupted

TABLE II. INTERVAL OF ANASTOMOSES AT TIME OF EXAMINATION

TYPE OF SUTURE	PLAIN			MATTRESS		
	CONTINUOUS	INTER- RUPTED	ALL	CONTINUOUS	INTER- RUPTED	ALL
Number of arteries sutured	1	23	45	27	4	51
Number examined in 10 days or less	9 (39%)	8 (36%)	17 (35%)	10 (37%)	8 (37%)	18 (35%)
Number examined in from 11 to 30 days	8 (33%)	9 (41%)	17 (38%)	10 (37%)	1 (50%)	22 (43%)
Number examined 30 days or more after operation	6 (26%)	5 (22%)	11 (24%)	7 (26%)	4 (100%)	11 (22%)
Average duration of anastomoses at time of examination, in days	26	23	24	4	19	22

mattress technique were examined in ten days or less and after thirty days or more and a correspondingly larger percentage in from eleven to thirty days. Of the forty-five arteries repaired with plain sutures, 38 per cent were examined in ten days or less, 38 per cent in from eleven to thirty days, and 24 per cent after thirty days or more. In the case of the fifty-one arteries anastomosed by mattress sutures these percentages were almost the same: 35, 43 and 22 per cent, respectively.

In Table III the data are given concerning the size of the arteries sutured. Very small arteries were used in only 20 per cent of those repaired with plain sutures, and in one-third of those repaired with mattress sutures. Since it is apparent that the chance of success is greater with larger vessels, it is clear that



TABLE 1. COMPARISON OF RESULTS OF E TO EMB ARRIVAL FOR

TYPE OF CASE	PLAID			V. TRAIL			TOTAL
	COUNT	PERCENT	ALL	COUNT	PERCENT	ALL	
Number of arrivals as used	1	92	43	97	4	91	96
Number threatened	6	3	4	5	4	4	17
Number with structure	3	4†		11	5	3	10
Number in structure	1	1	2	1	0	1	2
Number in structure	11		3	1	0	1	4
Number with complications	10 (41.2%)	(50.4%)	18 (40%)	7 (3.0%)	3 (9.9%)	12 (53.8%)	30 (41.5%)
Number without complications	12 (50.5%)	14 (61.6%)	37 (80%)	20 (74.1%)	19 (79.5%)	19 (70.0%)	46 (69.5%)

† One of the lesions was considered close to another lesion in the same patient.

One of these cases is also listed under thromboses.

These listed under thromboses.

One also listed under thromboses. The others had

This case is also listed under structure.

Number of lesions

Number of lesions

Number of lesions

In analyzing the results of this study it is important to make certain that the outcome in the various groups was dependent upon the type of suture used and not upon some other variable. Except for the difference in the suture technique, most of those factors which might conceivably influence the result were constant. The same artery was used, the same general operative technique, the same operators, and the needles, suture materials, and clamps were identical. Two factors, however, require analysis: the length of time between the arterial repair and the examination of the specimen and the size of the sutured artery. The first might be of some significance for although such complications as dehiscence and thrombosis undoubtedly occur early, others, such as strictures or aneurysm, might not be evident for some time after the procedure has been accomplished. The second is undoubtedly the most important variable which might influence the result.

In Table II data are listed concerning the interval of time which elapsed between the operative procedure and examination of the specimen. It will be seen that the duration of the anastomoses did not vary greatly in the different groups. The percentage of specimens examined in ten days or less, in from eleven to thirty days, and after thirty days or more was almost precisely the same in the groups repaired by continuous and interrupted plain and continuous mattress sutures. A slightly smaller percentage of those repaired by interrupted

TABLE II. INTERVAL OF ANASTOMOSES AT TIME OF EXAMINATION

	PLAIN			MATTRESS		
	CONTINUOUS	INTER- RUPTED		CONTINUOUS	INTER- RUPTED	ALL
			(%)			
				24	51	
				10 (37%)	8 (33%)	18 (35%)
Number examined in from 11 to 30 days	8 (33%)	9 (41%)	1 (3%)	10 (37%)	1 (6%)	22 (43%)
Number examined 30 days or more after operation	6 (26%)	3 (23%)	11 (44%)	(26%)	4 (16%)	11 (22%)
Average duration of anastomosis	26	23	24	4	19	22
Time of examination, days						

mattress technique were examined in ten days or less and after thirty days or more and a correspondingly larger percentage in from eleven to thirty days. Of the forty-five arteries repaired with plain sutures, 38 per cent were examined in ten days or less, 38 per cent in from eleven to thirty days, and 4 per cent after thirty days or more. In the case of the fifty-one arteries anastomosed by mattress sutures these percentages were almost the same: 3, 43 and 22 per cent respectively.

In Table III the data are given concerning the size of the arteries sutured. Very small arteries were used in only 20 per cent of those repaired with plain sutures, and in one-third of those repaired with mattress sutures. Since it is apparent that the chance of success is greater with larger vessels, it is clear that

TABLE 1. OTHER ACTIONS OF BARN OR E. TO EMB. UNIVERSAL BUN AS A CO. FIRST Dn Rn T IQ

TYPE OF ACTION	LAIN			TTS			TOTAL
	CONTINUED	INTERMITTENT	LI	UNITS	INTER	AI	
Number (actions entered)	47	23	43	27	4	51	84
Number (thrombosed)		2	8	5	4		17
Number (in striations)	1	4†	7	14	5	2	10
Number (in striations)	1	1		1	0	1	2
Number (in striations)	11	2	3	1	0	1	4
Number (in striations)	18 (47.5%)	13 (41%)	19 (60%)	7 (25.9%)	3 (20.4%)	12 (53.8%)	50 (31.5%)
Number (in striations)	12 (60.5%)	14 (60.9%)	47 (60%)	20 (74.1%)	10 (79.2%)	19 (78.5%)	69 (68.5%)

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any variation in the size of the vessel favored success in the group in which plain sutures were used. In order to analyze this important matter further the data presented in Table I are broken down in Table IV according to whether the sutured artery was larger or smaller than a diameter of 3.2 mm. It is evident that complications were more frequent when small arteries were sutured, the incidence varying from 37.5 per cent in the case of those repaired by interrupted mattress sutures to 60 per cent in the case of those repaired by the Carrel technique. There were complications in 4.1 per cent of the small arteries anastomosed with mattress sutures and in 5.5 per cent of those in which plain sutures were used. The number of small arteries sutured is too small to permit any conclusions concerning the relative merits of the various types of sutures. If anything the data suggest a trend toward fewer complications with interrupted mattress sutures. Comparison of the results with suture of larger vessels is more informa-

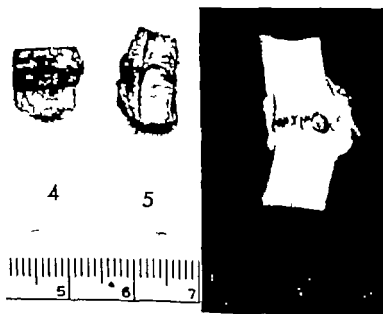


Fig. 1  
Gross  
appearance  
of a small  
aneurysm  
and of a  
stricture.

five sin  
results  
than in  
a plain sutures almost 90 per cent of the former hav  
ing healed without complications, while only 64 per cent of the latter healed  
without complication. In the group in which mattress sutures were used, compli-  
cation were limited to a few instances of thrombosis. In the other group  
there were examples of stricture aneurysm and debrisence as well.  
The gross appearance of a small aneurysm and of a stricture is shown in  
the photographs in Fig. 1. In Table V pertinent data are recorded concerning

TABLE III. COMPARISON OF DIAMETERS OF A VESSEL OBTAINED BY DIFFERENT SURVEY METHODS

TYPE OF BUTLER	PLAIN			MATTRESS		
	CORTEX	INTERRUPTED	ALL	CORTEX	INTERRUPTED	ALL
Number of arteries measured	23	22	43	27	4	61
Number with diameter 2 mm or less	5 (22%)	4 (18%)	9 (20%)	9 (33%)	8 (20%)	17 (28%)
Number with diameter 2 to 3 mm	10 (43%)	10 (45%)	20 (46%)	8 (30%)	9 (22%)	17 (28%)
Number with diameter 3 to 4 mm	8 (35%)	8 (36%)	16 (37%)	10 (37%)	2 (5%)	1 (2%)

TABLE IV. A. NUMBER OF RESULTS OF 35 TO 38 ARTERIAL SURVEYS ACCORDING TO METHOD OF BUTLER AND SIZE OF ARTERY

TYPE OF BUTLER	PLAIN			MATTRESS		
	CORTEX	INTERRUPTED	ALL	CORTEX	INTERRUPTED	ALL
Diameter of artery not less than 3.8 mm						
Number of arteries selected	14	14	28	18	16	34
Number thrombosed	2	2	4	2	5	7
Number with artery occluded	2	4	6	0	0	0
Number with diameter less than 3.8 mm	11	11	22	0	0	0
Number with complications	7 (50%)	6 (54%)	13 (59%)	2 (11%)	2 (12%)	4 (12%)
Number about complications	11 (79%)	18 (64%)	29 (64%)	16 (89%)	14 (88%)	30 (90%)
Diameter of artery 3.8 mm or less						
Number (arteries selected)	8	4	12	9	5	14
Number thrombosed	2	0	2	2	2	4
Number with artery occluded	0	0	0	1	1	2
Number with diameter less than 3.8 mm	0	0	0	1	0	1
Number with complications	7 (88%)	2 (50%)	9 (75%)	5 (56%)	3 (60%)	8 (57%)
Number about complications	2 (25%)	2 (50%)	4 (33%)	4 (44%)	5 (100%)	9 (64%)
One had aneurysm, another had partial obstructions and complete occlusions of branches						
One case had both obstructions and thromboses						
One listed under obstructions						

appear that these complications were directly related to the type of suture. Although such complications were nearly twice as common when small arteries were repaired (96.0 per cent as compared with 44.3 per cent) in the group of the larger vessels they occurred in ten of the thirty-six cases repaired with plain sutures (27.7 per cent) and in none of the thirty-four repaired with mattress sutures.

#### DISCUSSION

There can be no doubt that, regardless of the method of suture used in vascular repair certain fundamental principles must be followed if the best results are to be obtained. The vessel must be carefully stripped of adventitia so that the adventitia does not fall into the suture line and is not carried into the lumen by the sutures themselves. The vessel must be handled gently and trauma avoided. It must not be allowed to become dry during the procedure. Only fine needles and fine nonirritating nonabsorbable suture materials should be employed. It appears to be of some aid to keep the needle and suture well lubricated with mineral oil or moistened with saline solution. The vessel wall should be approximated with the intimal layer everted. Infection must be avoided.

Our studies would indicate that mattress sutures which fix the opposed ends of the vessel in a position of eversion are superior to plain sutures which bring the ends of the vessel together layer to layer. The superiority of the mattress technique is particularly evident in reference to the avoidance of such complications as dehiscence, aneurysm and strictures; there was no significant difference in the incidence of thrombosis with plain or mattress sutures. It must be emphasized, however, that thrombosis is the one common complication for which we have a fairly reliable counter measure—the utilization of anticoagulants. We employed no anticoagulants in the present study. Their usefulness in the prevention of thrombosis is suggested by clinical experience and is well established from experimental work. It is of interest that the recent experiment of Kieselwetter and Shumacker<sup>12</sup> reveal that heparin appears to be a better agent than dicumarol in the prevention of intra-arterial thrombosis. Fortunately anticoagulants can be used safely in operations upon the peripheral arteries.<sup>13</sup> They cannot be used with safety in operation within the thorax or peritoneal cavity. Fortunately, too, most of the vascular repairs within these cavities are either upon large vessels such as the aorta where the chance of thrombosis is not great, or are performed to produce a shunt from a high pressure to a low pressure area, where the rapid flow of blood also reduces the hazard of clotting. They can be used where they are most needed in the surgery of the peripheral vessel. It is significant that Gross and Hufnagel<sup>14</sup> found the continuous mattress suture superior to the continuous plain suture in experimental anastomosis of the aorta, bleeding from the suture line being rare with the former and common and troublesome with the latter method. We also noted less bleeding when mattress sutures were used. It would seem plausible that bleeding at the time the anastomosis is completed means in reverse the likelihood of subsequent complications.

Our studies demonstrate a fact which has appeared evident from other experimental and clinical work, namely, that the chance of success in arterial suture is definitely reduced when one is working with a vessel of extremely small

all the complications which occurred. These data simply confirm what is apparent from those already presented. Eight of the seventeen instances of thrombosis (47 per cent) were in arteries 3 mm in diameter or smaller whereas only 27 per cent of the arteries sutured were of such small diameter. The type of suture apparently was not a great factor in the incidence of thrombosis. With plain suture technique thrombosis took place in five of the thirty-six larger arteries and in three of the nine smaller arteries. With mattress sutures four of the thirty-four larger arteries were thrombosed and five of the seventeen smaller arteries. Three of these seventeen cases of thrombosis were in vessels which also had strictures. Excluding these three cases, six of the seven cases of stricture occurred with plain suture technique and only one with mattress technique. With these included, seven of the ten cases of stricture followed anastomosis with plain sutures. Two of the three instances of aneurysm and three of the four examples of dehiscence similarly occurred with plain suture technique. It would thus

TABLE V. A SUMMARY OF COMPLICATIONS FOLLOWING END-TO-END ANASTOMOSES OF ARTERIES

COMPLICATIONS	DIAMETER OF ARTERY (IN MM.)	PERCENT OF ANASTOMOSES (IN PERCENT)	DEGREE	TYPE OF REPAIR	COMMENTS
T	3.5	5	Mild	CP	
T	4.0	23	Severe	CP	
T	4.0	33	Severe	IP	
T	4.5	4	Mild	IP	Also stricture
T	4.5	7	Mild	OP	
T	3.2	72	Severe	IM	
T	3.5	24	Severe	IM	
T	3.3	71	Severe	OM	
T	4.0	8	Mild	CM	
T	1.0	14	Severe	CP	
T	1	9	Severe	CP	
T	5	41	Severe	CP	
T	1.0	19	Severe	OM	
T	3.0	15	Severe	OM	Also stricture
T	3.2	1	Severe	CM	
T	2.0	15	Mild	IM	Also stricture
T	2	17	Severe	IM	
B	4.5	41	Moderate	IP	
B	4.0	59	Severe	IP	
B	4.0	70	Severe	IP	
B	4.5	4	Mild	IP	Also thrombosis
B	4.5	41	Severe	CP	Complete occlusion
B	4.0	66	Severe	CP	
B	4.3	74	Severe	CP	Partial dehiscence
B	1.0	13	Moderate	CM	Also thrombosis
B	2.5	34	Severe	IM	
B	1	17	Moderate	IM	Also thrombosis
A	4.2	20	Very small	CP	
A	4	40	Very small	IP	
A	3.0	7	Very small	CM	
D	4.3	76	Partial	CP	Also stricture
D	2.5	57	Complete	IP	
D	2.5	41	Complete	IP	
D	3.0	4	Complete	CM	

T, Thrombosis.

B, Stricture.

A, Aneurysm.

D, Dehiscence.

CP, Continuous plain.

IP, Interrupted plain.

OM, Ombudsman mattress.

IM, Interrupted mattress.





was Too few anastomoses were performed upon such small arteries to yield significant data concerning the relative merit of the various suture techniques.

Although the experiment demonstrated a significant advantage of the mattress over the plain sutures, there was no convincing evidence that the interrupted sutures were superior to the continuous sutures or vice versa. In actual practice there also seems to be little advantage of one method over the other. Theoretically continuous sutures have the disadvantage that they may be drawn too tightly and thus may produce some constriction. Should a continuous suture break it would obviously subject the anastomosis to greater chance of disruption. Continuous sutures, on the other hand, are placed with little more ease and rapidity. In patients, it has been the practice of one of us (H B S Jr) to use interrupted mattress sutures where the vessels are easily accessible as in the case of the peripheral arteries, and continuous mattress sutures in procedures where approximation is more difficult and where there is poor access to certain portions of the suture line once the anastomosis is completed, as in the Blalock operation and in coarctation of the aorta.

It should be pointed out that the neck was not splinted in any of our animal. It is entirely likely that proper splinting to avoid any strain upon the suture line might have influenced the results favorably. In other experiments we have found that the recently sutured vessel will withstand, without leaking or bursting, intraluminal pressures far in excess of the systolic blood pressure even in hypertensive states. They can, however, be pulled apart by a relatively small force directly applied.

It must be emphasized that normal arteries were used in these experiments and that the anastomoses were performed by operators who had considerable experience with methods of vascular repair. It is not unlikely that the advantage of the mattress technique which was evident in our experiments might be amplified in arterial surgery upon somewhat damaged diseased arteries in man, or in the hands of operators with relatively small experience in vascular suture techniques.

#### CONCLUSIONS

The experiment reported demonstrates that end-to-end arterial repair is attended by a fairly high incidence of complications when small arteries are used, irrespective of the type of suture. With arteries of moderate size the incidence of thrombosis does not vary greatly with different methods of repair but other complications such as dehiscence, stricture and aneurysm are much less frequent when everting mattress sutures are used. It is believed that mattress techniques will prove most reliable in major arterial use of antithrombotics, of antibiotics or chemotherapeutic agents when indicated, and of proper splinting when necessary to avoid undue stress on the repaired anastomosis of arteries.

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The animals were kept on a routine kennel diet and water ad lib throughout the entire experiment except during the periods of irrigation. No medications except intravenous calcium gluconate were given.

*Method of Irrigation*—A Foley type catheter was placed in each end of the intestinal segment. The wash fluid was allowed to drip into the proximal end from an overhead reservoir and collected from the distal end in a earboy. During the irrigation periods the dogs were placed on an animal table and maintained in position by means of loose restraining bands. The rate of flow of the wash fluid was from 6 to 66 cc per minute. Four different fluids were used: (1) normal NaCl; (2) 3 per cent NaCl; (3) NaCl 61 Gm, CaCl<sub>2</sub> 0.23 Gm, CaHPO<sub>4</sub> 0.0 Gm and Na<sub>2</sub>SO<sub>4</sub> 10 Gm per liter of solution; and (4) NaCl 61 Gm, CaCl<sub>2</sub> 0.23 Gm, KCl 0.3 Gm, NaHCO<sub>3</sub> 9 Gm, Na<sub>2</sub>SO<sub>4</sub> 30 Gm and glucose 10 Gm per liter of solution.

Irrigation was intermittent and was begun 21 to 30 hours after nephrectomy. Single irrigation period lasted from 3 to 10.5 hours. No animal was irrigated more than 10.5 hours in any one 4-hour period.

*Chemistry*—In the control animals, blood urea nitrogen and nonprotein nitrogen determination were made twice a day. In the irrigated animals the blood urea nitrogen, nonprotein nitrogen and hematocrit values were determined at the beginning and end of each irrigation period. Urea nitrogen and nonprotein nitrogen values were determined on each sample of wash fluid. Duplicate determinations were made as a check in each case. Heparin was used as the anticoagulant for all blood samples. Urea and nonprotein nitrogen determination were done by a modified Gentrakow method. The Van Allen hematocrit tube was used in determining the hematocrit values. Since the urea and nonprotein nitrogen values paralleled one another closely only the urea nitrogen values will be presented here.

## RESULTS

As was to be expected both the control and the irrigated dogs showed a considerable weight loss between the formation of the Thiry Vella fistula and the nephrectomy. Actual weight loss varied from 1.2 to 7.8 kilograms and the percentage weight loss varied from 11 to 47 per cent. The irrigated animals lost on an average 16 per cent more weight than the controls. No correlation could be found between the weight loss and the survival time. However the three irrigated dogs which averaged the longest survival time also averaged the greatest loss in weight (37 per cent).

There were five control dogs used in these experiments. The survival time after nephrectomy ranged from 3 to 104 hours with an average of 73 hours. The terminal blood urea nitrogen level varied from 145 to 265 mg per cent with an average of 193 mg per cent. The average rate of rise of the urea nitrogen was 5 mg per cent per hour.

Uremic symptoms appeared in most of the control animals at 36 to 48 hours after nephrectomy and were clinically manifested at about 60 hours. Actual convulsions did not supervene until shortly before death. At autopsy none of the animals

## THE TREATMENT OF EXPERIMENTAL UREMIA BY INTESTINAL LAVAGE

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RECENTLY several investigators have attempted to develop a practical means of removing retention products in cases of acute renal failure. The search for such a means is predicated on the theory that given time the kidneys may be able to recover function that has been temporarily damaged by such means as transfusion reactions, sulfonamide toxicity, the crush syndrome, toxemia of pregnancy, mercury poisoning and surgical trauma to the urinary tract.

Three main methods for the removal of retention products have been investigated: (1) peritoneal lavage,<sup>1,2</sup> (2) dialysis of the blood outside the body and returning it to the circulation,<sup>3</sup> and (3) intestinal lavage.<sup>4-6</sup> The first two methods have received more attention than has intestinal lavage and already have been given a clinical trial with varying degrees of success. The clinical use of intestinal lavage has been very limited and has received relatively little attention. Except for the work of Kolff and Bliss,<sup>7</sup> the experimental side has been neglected.

This communication deals with the experimental results obtained from the lavage of isolated intestinal loops in dogs rendered uremic by means of bilateral nephrectomy. This problem was suggested to one of us (H. N. H.) by the late Dr. Edmund Andrews in 1934 and a few very preliminary experiments were carried out at that time.

### METHOD

*Preparation of the Animals*.—The animals used in these experiments were healthy mongrel dogs weighing from 5.5 to 17 kilograms. Under nembutal anesthesia, intestinal segments with attached mesentery and blood supply were isolated and each end of the segments was sutured to the abdominal wall and skin so as to form a T-tube. Continuity of the intestine was restored by an end-to-end anastomosis. The length of these segments varied from 20 to 40 inches. In the animals included in this series, the proximal end was approximately 5 inches below the ligament of Treitz. Eleven to fourteen days later when the incisions had thoroughly healed, bilateral nephrectomy was done under ether anesthesia through bilateral paravertebral incisions.

TABLE I. RESULTS OBTAINED IN 1 TEST AL LAVAGE

DOG	LOOP LENGTH (IN.)	PER CENT VITALITY (PER.)	NR. WASHES	BLOOD UREA NITROGEN (MG.)		HEMATOCRIT		UREA NITROGEN REMOVED (M.)		BLOOD UREA	UREA NITROGEN IN WASH FLUID (MG. C.)
				IN IT.	PER CENT	IN IT. L.	PER CENT	TOT. L.	PER INCH		
1	21	63.5	4	141	14	60	53	403	3	1	3.8
				14	150	33	57	615	9	2	7.7
25	20	63	5	51	53	40	40	223	8.4	1	6.4
			3	53	53	40	40	103	3.6	1	3.3
			23	57	61	40	40	240	3.6	1	7
			6	70	94	33	20	862	4.8	1	4.9
			4	94	93	29	23	34	3.1	1	9
29	27	72	10.5	49	51	41	39	971	3.5	3	4.0
				62	69	36	28	1417	3.6	3	4.4
22	20	92.3	7	114	14	44	43	1473	10.3	4	9
			6	166	163	46	44	1440	14	4	8
			33	201	223	41	43	622	8.9	4	7
44	24	96	7	64	53	1	34	1000	8.8	3 (Reused)	20
			7	80	70	32	29	1440	8.8	3 (Reused)	29
			7	14	11	23	31	400	1.5	3 (Reused)	3
48	25	80	7	45	34	25	23	900	3.6	3 (Reused)	13
			63	2	86	23	23	800	3.6	3 (Reused)	34
			33	113	114	—	20	130	1.3	3 (Reused)	39

reused and during one period only 1.3 mg. were removed per inch per hour. At the time when this low return occurred the wash fluid contained between 34 and 39 mg. per cent of urea nitrogen. A similar low value occurred in Dog 44 when there was 29 to 37 mg. per cent of urea nitrogen in the reused wash fluid.

Best results were obtained with hypertonic fluid when 3 per cent saline solution was used alone or when 1 per cent sodium sulfate was added to the wash fluid and 1 liter of more urea nitrogen was then removed. Apparently some urea is excreted actively into the lumen of the bowel during the resting phase, since when the bowel is washed clean of urea with water a small amount can be obtained from the lumen several hours later (Table II). It is felt that the hypertonic solution accelerates the excretion by producing a chemical or physical irritation of the mucosa rather than by a purely osmotic process. This excretion does not appear to be perceptibly accelerated by a high blood urea level but rather is a constant slow process.

As can be seen in Dogs 44 and 48 (Table I) a high urea content in the wash fluid does not show the amount of urea removed from the blood stream. This

TABLE II. EXCRETION OF UREA BY THE RESTING SMALL BOWEL.

DOG	LOOP LENGTH (IN.)	BLOOD UREA NITROGEN (MG. C.)	TIME (MIN.)	UREA NITROGEN EXCRETED INTO LOOP (MG. C.)
27	34	3.5	17	7
3	25	1	4	10
4	25	11.3	4	7
4	24	1	4	1
1	1	14	4	10
16	34	15	48	30
2	23	17.7	62	10
1	24	16.6	73	30
1	23	12.1	41	20
		3	101	20

showed gross edema and only one appeared to be slightly dehydrated. The length of the loops in the control group had no effect on the survival time.

The data on the irrigation experiments are shown in Table I. A graphic representation of the results obtained in one dog (No. 41) is shown in Fig. 1. Eighteen irrigation experiments were carried out in six dogs. The results in three other dogs are excluded, since at autopsy two of these had bilateral bronchopneumonia and the other had a large abscess in each nephrectomy incision. Two of the diseased animal had low ileal loops in which the distal end was 5 inches proximal to the ileocecal valve. A appreciable difference in the amount of urea removed by lavage could be attributed to the site of the loop. In those six irrigated dogs used as the basis for this report, the average survival time was 81 hours, only 8 hours longer than that of the controls. The survival times ranged from 63 to 99 hours. The terminal blood urea nitrogen levels ranged from 89 to 220 mg. per cent, with an average of 144 mg. per cent. This is 40 mg. per cent lower than the average terminal urea nitrogen level in

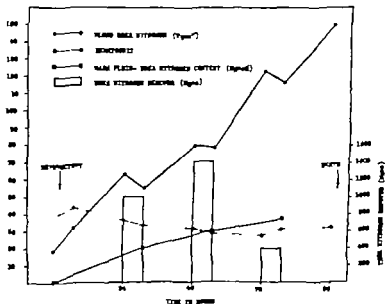


Fig. 1.—Results of Irrigation in Dog No. 41.

the controls. The average rate of removal of the urea nitrogen was 1.6 mg. per cent per hour during the entire survival period, including both the irrigation and the non-irrigation period. The blood urea nitrogen was kept level or was lowered 1 to 8 mg. per cent during the actual irrigation period in 8 of 44.5 per cent, of the experiments. In 10 or 65.5 per cent, the urea nitrogen rose 1 to 25 mg. per cent. The maximum efficiency of urea removal was in Dog 42 where 14 mg. of urea nitrogen were removed per inch of intestine per hour of irrigation. The poorest result was obtained in Dog 48 where the wash fluid was

In a 36 inch segment this would amount to about 19 Cm of urea in 24 hours. While this is less than can be obtained by peritoneal lavage it is a significant amount.

The exact nature and cause of the irrigation syndrome encountered in these animals are not entirely clear. This syndrome is probably based on an electrolyte upset. That hypocalcemia plays a part is evident from the slight improvement following intravenous calcium. It seems logical to assume that the electrolyte upset itself is at least partially due to the selective absorption of the intestine since this organ by no means acts as a simple semipermeable membrane. Hence a fluid which is ideal for peritoneal lavage could not be expected to perform a well in intestinal lavage. The main difficulty to be overcome consists in finding a wash fluid which will not disturb the electrolyte and fluid balance and at the same time will allow a maximum diffusion or excretion of urea into the bowel. On the basis of these experiments it is difficult to prognosticate what the final composition of that fluid will be. It is probably safe to state that hypertonic fluid, a poorly absorbed substance such as sodium or magnesium sulfate should be present to aid in the removal of greater amounts of urea and to prevent edema.

Clinically of course, it would not be feasible surgically to isolate small bowel loops. If with further investigation the procedure shows greater promise, irrigation could be carried out with a modified Miller-Abbott tube as was used by Goudant.

#### SUMMARY

1 The results of experiments with intestinal lavage in experimental uremia are presented.

The prolongation of life in the irrigated animals as compared to the control animals is not significant probably because of a severe upset in the electrolyte pattern.

3 Fairly large amounts of urea can be removed by intestinal lavage but the problem of electrolyte balance remains to be solved.

4 The possibility of more widespread clinical application is mentioned.

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was also evident in several other dogs which are not included in this communication.

In only three of the washing experiments did the hematocrit rise during the actual irrigation period. In the remainder the hematocrit stayed level or dropped one to five points. Hence even though the wash fluid was hypertonic, these animals were able to extract water from it. From 50 to 30 cc less fluid were recovered than was originally used.

Extensive chemical analyses were not performed so we were unable to follow the fluid and electrolyte pattern. It was very obvious that this was markedly disturbed. Some of the animals that appeared to be in good condition at the beginning of the irrigation period later showed marked muscular incoordination and irritability, tremors, convulsions, and vomiting. After the irrigation was completed, they were unable to stand or walk and appeared completely disoriented. This condition occurred even when the blood urea nitrogen remained level or was lowered. Moderate recovery occurred in the overnight rest periods between irrigations. Large doses of calcium gluconate intravenously gave only partial relief. In those cases where the wash fluid was reused through out the survival time this symptom complex was much less apparent. This picture seems to resemble somewhat that seen in animals fed sea water.<sup>4,12</sup> Further studies are under way to determine the cause of these symptoms and to obtain a comprehensive picture of the electrolyte pattern.

#### DISCUSSION

The results obtained with intestinal lavage by various workers have been conflicting. Seligman and associates<sup>8</sup> estimated that ten feet of bowel as an isolated segment would be required to supply 10 per cent of the maximum normal renal clearance (75 ml per minute). In one uremic patient they were able to extract not more than 1 Gm of urea in a 4 hour period by gastroduodenal suction. In this same patient irrigation of 10 inch isolated loop of ileum removed only 0.1 Gm of urea in 4 hours. Blum and co-workers<sup>13</sup> found gastroduodenal irrigation in uremic dogs disappointing.

On the other hand, Golin et al.<sup>14</sup> was able to remove 10 Gm of urea in 7½ hours by forced testicular irrigation with hypertonic sodium sulfate solution. He stated that there were no significant changes in the blood urea level. Schurer<sup>9</sup> mentioned two cases of renal shutdown following incompatible blood reaction in which gastro-lavage was instituted. In both cases the serum nitrogen in the blood was lowered and maintained at a low level for 10 and 14 days, respectively. Both patients recovered. Kolff<sup>15</sup> was able to remove as much as 5 Gm of urea in 10 hours by perfusion of an ileal loop one meter long.

We believe from our small number of experiments that intestinal lavage can produce lowering of the blood urea nitrogen, significant removal of urea, and that fairly large amount of urea can be removed. Taking the result of one of the experiments in Dog 28 as all of them. Dog 32 as representative (hypertonic fluid was used in these experiments) one could expect to remove 250 mg of urea nitrogen per 4 hours per inch of intestine irrigated. 1

In a 36 inch segment this would amount to about 19 Gm of urea in 24 hours. While this is less than can be obtained by peritoneal lavage it is a significant amount.

The exact nature and cause of the irrigation syndrome encountered in these animals are not entirely clear. This syndrome is probably based on an electrolyte upset. That hypocalcemia plays a part is evident from the slight improvement following intravenous calcium. It seems logical to assume that the electrolyte upset itself is at least partially due to the selective absorption of the intestine since this organ by no means acts as a simple semipermeable membrane. Hence a fluid which is ideal for peritoneal lavage could not be expected to perform as well in intestinal lavage. The main difficulty to be overcome consists in finding a wash fluid which will not disturb the electrolyte and fluid balance and at the same time will allow maximum diffusion or excretion of urea into the bowel. On the basis of these experiments it is difficult to prognosticate what the final composition of that fluid will be. It is probably safe to state that hypertonicity due to a poorly absorbed substance such as sodium or magnesium sulfate should be present to aid in the removal of greater amounts of urea and to prevent edema.

Clinically of course it would not be feasible surgically to isolate small bowel loops. If with further investigation, the procedure shows greater promise, irrigation could be carried out with a modified Miller Abbott tube as was used by Goudswaard.

#### SUMMARY

1. The results of experiment with intestinal lavage in experimental uremia are presented.
2. The prolongation of life in the irrigated animals as compared to the control animals is not significant probably because of a severe upset in the electrolyte pattern.
3. Fairly large amounts of urea can be removed by intestinal lavage but the problem of electrolyte balance remains to be solved.
4. The possibility of more widespread clinical application is mentioned.

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# THE NEUTRALIZATION OF HEPARIN BY PROTAMINE

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THERE has been little interest in an antidote for heparin, probably because the simple expedient of stopping its administration is followed by a restoration of the normal clotting time of the blood in an hour or two. Nevertheless, it is easy to imagine situations where it would be desirable to correct a hemorrhagic tendency in a matter of minutes rather than hours. In 1937, Chargoff and Olson reported that the activity of heparin could be entirely stopped by the intravenous injection of a protamine (salmine from salmon spermatozoa). They were investigating the antieagulant properties of heparin and attempted to prolong its transient action by combining it with another substance. They reasoned that if protamine delayed the absorption of insulin it might do the same for heparin. However, they found that the effect of heparin was nullified by the protamine. Apparently the two substances form a stable salt which has a low degree of dissociation.

The experimental work on dogs was applied to human beings by Jorpes, Flman and Thaning. They neutralized the effect of heparin in ten individuals by giving the protamine, lupeme (from the herring) in the amount of 60 mg. for each 100 mg. of heparin.

The American literature contains no record of protamine being employed to counteract the action of heparin. Instead there are two statements which would discourage its use. In a review of the subject of heparin, Mason said: "Protamine is not of almost real in any form intravenously." The same statement occurred in a recent review of the literature on the management of arterial embolism. Therefore it seemed desirable to repeat a part of the work of the other investigators. We were particularly interested to see if an antiprotamine could be available in this country.

Two preparations of protamine were used in the experiment. We were supplied with some samples of the solution used by the Swedish group. This consisted of a per cent solution of protamine sulfate (lupeme). Presumably this was prepared according to the method described by Jorpes. The pure protamine sulfate from herring or salmon is dissolved in diluted hydrochloric acid pH 3, and sterilized in an autoclave. It produces no undesirable reactions. The material used in most of the experiment was prepared by dissolving protamine sulfate (salmine) to make a per cent solution. Sterilization was obtained by passing it through Berkefeld filter and phenol (1:10000) (1 per cent) was added as a preservative.

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Experiments were carried out on six dogs varying in weight from 10 to 30 kilograms. A sample of blood was withdrawn for the determination of the normal clotting time after which heparin (1 mg per kilogram) was injected through the same needle. The clotting time was determined by the Lee and White method (in erosion of test tubes). Twenty minutes after the injection of heparin a second sample of blood was withdrawn and protamine sulfate, 1 mg per kilogram, was injected through the same needle. Six to ten minutes after this injection, the third clotting time was obtained. On a subsequent day the animals were given identical injections of heparin and their clotting times were taken at thirty minute interval to determine the duration of the normal heparin effect.

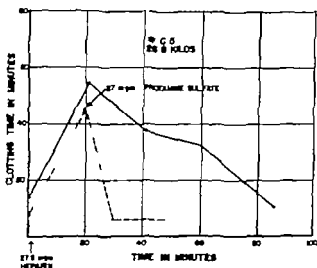


Fig. 1—Results of typical experiment on dog. Solid line indicates the effect of heparin alone. The broken line represents an experiment on different day showing the neutralization of heparin by protamine.

Similar results were obtained in each of the six experiments. The heparin injection caused a marked increase in the clotting time, an effect which was immediately abolished by the protamine. The findings of a typical experiment are shown in Fig. 1.

To investigate toxicity, was injected a small dose of protamine (200 mg for a dog weighing 40 kilograms). The animal became very excited and confused, but recovered from this reaction about one minute and subsequently showed no deviation from the normal. The clotting time remained near its normal level (eleven minutes) for one-half hour and then dropped to six minutes. Smaller doses (1 mg per kilogram) did not change the clotting time to normal dogs.

Since no adverse symptom were observed in the animal experiments, we extended the tests to man. The results obtained in five individuals are shown in Table I. It will be noted that in every instance the markedly elevated clotting time was brought to normal by the protamine injection.

TABLE I REDUCTION OF CLOTTING TIME BY PROTAMINE IN FIVE HEPARINIZED PATIENTS (CLOTTING TIME IN MINUTES)

CASE	WEIGHT (KG)	NORMAL CLOTTING TIME	IN FIBRIN	CLOTTING TIME 30 MIN. LATER	MO PROT. MIN.	CLOTTING TIME 8 MIN. LATER
1	55	18	50	120	50	18
	64	15	54	120	54	10
2	80	1	80	90	80	8
4	66	10	80	120	66	17
5	50	1	30	7	50	15

### CONCLUSIONS

We have corroborated the findings of previous investigators that protamine sulfate can be used to neutralize the anticoagulant effect of heparin. A non-toxic solution for intravenous use can be easily prepared.

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Experiments were carried out on six dogs varying in weight from 10 to 30 kilogram. A sample of blood was withdrawn for the determination of the normal clotting time after which heparin (1 mg per kilogram) was injected through the same needle. The clotting time was determined by the Lee and White method (inversion of test tubes). Twenty minutes after the injection of heparin a second sample of blood was withdrawn and protamine sulfate, 1 mg per kilogram, was injected through the same needle. Six to ten minutes after this injection, the third clotting time was obtained. On a subsequent day the animals were given identical injections of heparin and their clotting times were taken at thirty minute intervals to determine the duration of the normal heparin effect.

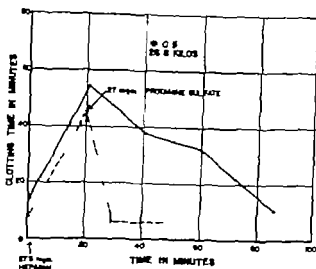


FIG. 1.—Results of typical experiment on dog. Solid line indicates the effect of heparin alone. The broken line represents an experiment on different day showing the neutralization of heparin by protamine.

Similar results were obtained in each of the six experiments. The heparin injection caused a marked increase in the clotting time, an effect which was immediately abolished by the protamine. The findings of a typical experiment are shown in Fig. 1.

To investigate toxicity we injected a massive dose of protamine (200 mg for a dog weighing 20 kilograms). The animal became very excited and confused, but recovered from this reaction in about ten minutes and subsequently showed no deviation from the normal. The clotting time remained on its normal level (eleven minutes) for one-half hour and then dropped to six minutes. Smaller doses (1 mg per kilogram) did not change the clotting time to normal dogs.

Since no adverse symptoms were observed in the animal experiments, we extended the tests to man. The results obtained in five individuals are shown in Table I. It will be noted that in every instance the markedly elevated clotting time was brought to normal by the protamine injection.

TABLE I. REDUCTION OF CLOTTING TIME BY PROTAMINE IN FIVE HEPARINIZED PATIENTS (CLOTTING TIME MINUTES)

CASE	WEIGHT (KG.)	NORMAL CLOTTING TIME	HEPARIN	CLOTTING TIME 90 MIN. LATER	HEPARIN	CLOTTING TIME 8 MI. LATER
1	65	10	54	120	60	15
	54	15	54	120	54	20
2	80	13	80	00	80	8
4	66	19	40	120	66	17
5	60	12	30	72	60	15

#### CONCLUSIONS

We have corroborated the findings of previous investigators that protamine sulfate can be used to neutralize the anticoagulant effect of heparin. A non-toxic solution for intra-venous use can be easily prepared.

#### REFERENCES

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## PATELLA FRACTURES

### A METHOD OF WIRING

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**B**ECAUSE of the fact that the incidence of fractured patella is rather common and usually there is a long and complicated convalescence, this study was instigated to seek a better method for treatment of fractured patella in which there is a definite separation of the fragments.

During the five years from June 1941, to June 1946 we treated 4 fresh fractured patellae in addition to 22 old refracted cases primarily from the seas, Army hospitals, and ship surgeons. Of the 24 fresh patella fractures, 30 were wired by the method described here. This study does not include ligamentous tear about the patella without fractures.

The selection of wiring cases had no prerequisite. The main fragments had to show  $\frac{1}{4}$  inch or more separation. All fractures showing less than  $\frac{1}{4}$  inch separation of main fragment were treated by closed reduction and cast.

A comparative study was carried out using patellectomy, partial patellectomy, screw fixation, Kirschner wire and various methods of wiring, suturing, and turnbuckle clamps.

### METHOD

A Kocher incision is used on the knee and reflected up and out. The rent of the capsule or the area where the anterior capsule is relaxed due to separation of the fragments, is located and opened transversely. The quadriceps expanded from the lateral border to a distance of one inch from the fracture site of either pole. Following wound closure the edges of the fractured fragment are curetted and approximation is checked for smooth closure. Using a No. 1 bit a hole is drilled transversely across the main fragment  $\frac{1}{4}$  inch from the fractured end and slightly eccentric to the frontal plane. Care is taken that the drill holes do not enter on the posterior patellar articular cartilage (Fig. 1). By use of an awl, the No. 1 stainless steel wire is passed through the 2 drill holes, on a loop manometer and the free end is then passed through the mid front attachment of the quadriceps on the patella in a circumferential manner and then in the same way through the patella tendon. In each instance the wire must hug the circumferential border of the patella at its mid position. The wire ends are then rounded to the place of bone insertion. As the wire is made taut by the surgeon at the anatomic aspect, the smooth gliding posterior surface of the patella for the anatomic reduction, and then several turns of wire are made both anterior and posterior for fixation. The free wire ends are cut at a stump of  $\frac{1}{4}$  inch. The wire ends must not infringe upon the anterior margin of the patella. The capsule is sutured with No. 1 chrome gut with 000 black silk to the skin.

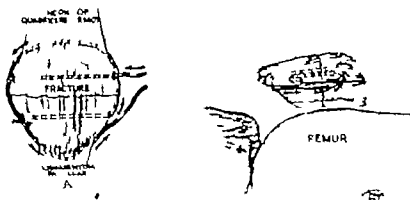


Fig 1—Position of drill holes and direction of wires. (From the Orthopaedic Service of the United States Marine Hospital, Stapleton, Staten Island)

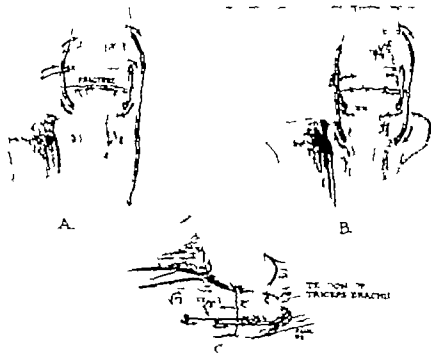


Fig 2—Wiring of fracture. A. Superior view of patella. B. Lateral view of patella. C. Superior view of patella. (From the Orthopaedic Service of the United States Marine Hospital, Stapleton, Staten Island)





Fig 1—A X-ray showing defects B after brain graft.

to resemble the normal supra-orbital ridge. These are inserted in the bed formed by the subperiosteal exposure of the frontal bone in the region of the defect. Small chips are placed around the graft to complete the filling of the deformity. After proper contour is secured a dental modeling compound impression of the area is made. It is allowed to harden and is relieved with firm pressure. This firm pressure by a smooth surface prevents any irregularities and maintains the contour. This is worn for three to four weeks.

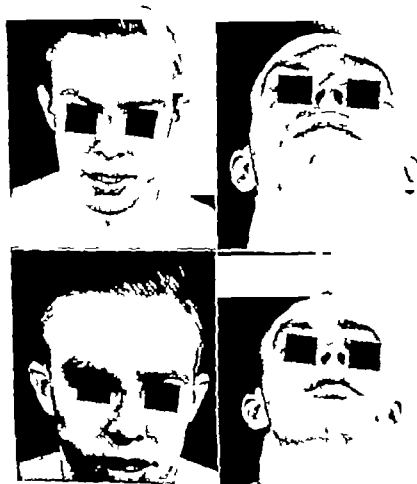


Fig. 1. (a) (b) (c) (d) Used by cancellous bone for defect of right supra-orbital region and frontal bone. (e) (f) (g) (h) (i) (j) (k) (l) (m) (n) (o) (p) (q) (r) (s) (t) (u) (v) (w) (x) (y) (z) (aa) (ab) (ac) (ad) (ae) (af) (ag) (ah) (ai) (aj) (ak) (al) (am) (an) (ao) (ap) (aq) (ar) (as) (at) (au) (av) (aw) (ax) (ay) (az) (ba) (bb) (bc) (bd) (be) (bf) (bg) (bh) (bi) (bj) (bk) (bl) (bm) (bn) (bo) (bp) (bq) (br) (bs) (bt) (bu) (bv) (bw) (bx) (by) (bz) (ca) (cb) (cc) (cd) (ce) (cf) (cg) (ch) (ci) (cj) (ck) (cl) (cm) (cn) (co) (cp) (cq) (cr) (cs) (ct) (cu) (cv) (cw) (cx) (cy) (cz) (da) (db) (dc) (dd) (de) (df) (dg) (dh) (di) (dj) (dk) (dl) (dm) (dn) (do) (dp) (dq) (dr) (ds) (dt) (du) (dv) (dw) (dx) (dy) (dz) (ea) (eb) (ec) (ed) (ee) (ef) (eg) (eh) (ei) (ej) (ek) (el) (em) (en) (eo) (ep) (eq) (er) (es) (et) (eu) (ev) (ew) (ex) (ey) (ez) (fa) (fb) (fc) (fd) (fe) (ff) (fg) (fh) (fi) (fj) (fk) (fl) (fm) (fn) (fo) (fp) (fq) (fr) (fs) (ft) (fu) (fv) (fw) (fx) (fy) (fz) (ga) (gb) (gc) (gd) (ge) (gf) (gg) (gh) (gi) (gj) (gk) (gl) (gm) (gn) (go) (gp) (gq) (gr) (gs) (gt) (gu) (gv) (gw) (gx) (gy) (gz) (ha) (hb) (hc) (hd) (he) (hf) (hg) (hh) (hi) (hj) (hk) (hl) (hm) (hn) (ho) (hp) (hq) (hr) (hs) (ht) (hu) (hv) (hw) (hx) (hy) (hz) (ia) (ib) (ic) (id) (ie) (if) (ig) (ih) (ii) (ij) (ik) (il) (im) (in) (io) (ip) (iq) (ir) (is) (it) (iu) (iv) (iw) (ix) (iy) (iz) (ja) (jb) (jc) (jd) (je) (jf) (jg) (jh) (ji) (jj) (jk) (jl) (jm) (jn) (jo) (jp) (jq) (jr) (js) (jt) (ju) (jv) (jw) (jx) (jy) (jz) (ka) (kb) (kc) (kd) (ke) (kf) (kg) (kh) (ki) (kj) (kk) (kl) (km) (kn) (ko) (kp) (kq) (kr) (ks) (kt) (ku) (kv) (kw) (kx) (ky) (kz) (la) (lb) (lc) (ld) (le) (lf) (lg) (lh) (li) (lj) (lk) (ll) (lm) (ln) (lo) (lp) (lq) (lr) (ls) (lt) (lu) (lv) (lw) (lx) (ly) (lz) (ma) (mb) (mc) (md) (me) (mf) (mg) (mh) (mi) (mj) (mk) (ml) (mm) (mn) (mo) (mp) (mq) (mr) (ms) (mt) (mu) (mv) (mw) (mx) (my) (mz) (na) (nb) (nc) (nd) (ne) (nf) (ng) (nh) (ni) (nj) (nk) (nl) (nm) (nn) (no) (np) (nq) (nr) (ns) (nt) (nu) (nv) (nw) (nx) (ny) (nz) (oa) (ob) (oc) (od) (oe) (of) (og) (oh) (oi) (oj) (ok) (ol) (om) (on) (oo) (op) (oq) (or) (os) (ot) (ou) (ov) (ow) (ox) (oy) (oz) (pa) (pb) (pc) (pd) (pe) (pf) (pg) (ph) (pi) (pj) (pk) (pl) (pm) (pn) (po) (pp) (pq) (pr) (ps) (pt) (pu) (pv) (pw) (px) (py) (pz) (qa) (qb) (qc) (qd) (qe) (qf) (qg) (qh) (qi) (qj) (qk) (ql) (qm) (qn) (qo) (qp) (qq) (qr) (qs) (qt) (qu) (qv) (qw) (qx) (qy) (qz) (ra) (rb) (rc) (rd) (re) (rf) (rg) (rh) (ri) (rj) (rk) (rl) (rm) (rn) (ro) (rp) (rq) (rr) (rs) (rt) (ru) (rv) (rw) (rx) (ry) (rz) (sa) (sb) (sc) (sd) (se) (sf) (sg) (sh) (si) (sj) (sk) (sl) (sm) (sn) (so) (sp) (sq) (sr) (ss) (st) (su) (sv) (sw) (sx) (sy) (sz) (ta) (tb) (tc) (td) (te) (tf) (tg) (th) (ti) (tj) (tk) (tl) (tm) (tn) (to) (tp) (tq) (tr) (ts) (tt) (tu) (tv) (tw) (tx) (ty) (tz) (ua) (ub) (uc) (ud) (ue) (uf) (ug) (uh) (ui) (uj) (uk) (ul) (um) (un) (uo) (up) (uq) (ur) (us) (ut) (uu) (uv) (uw) (ux) (uy) (uz) (va) (vb) (vc) (vd) (ve) (vf) (vg) (vh) (vi) (vj) (vk) (vl) (vm) (vn) (vo) (vp) (vq) (vr) (vs) (vt) (vu) (vv) (vw) (vx) (vy) (vz) (wa) (wb) (wc) (wd) (we) (wf) (wg) (wh) (wi) (wj) (wk) (wl) (wm) (wn) (wo) (wp) (wq) (wr) (ws) (wt) (wu) (wv) (ww) (wx) (wy) (wz) (xa) (xb) (xc) (xd) (xe) (xf) (xg) (xh) (xi) (xj) (xk) (xl) (xm) (xn) (xo) (xp) (xq) (xr) (xs) (xt) (xu) (xv) (xw) (xx) (xy) (xz) (ya) (yb) (yc) (yd) (ye) (yf) (yg) (yh) (yi) (yj) (yk) (yl) (ym) (yn) (yo) (yp) (yq) (yr) (ys) (yt) (yu) (yv) (yw) (yx) (yy) (yz) (za) (zb) (zc) (zd) (ze) (zf) (zg) (zh) (zi) (zj) (zk) (zl) (zm) (zn) (zo) (zp) (zq) (zr) (zs) (zt) (zu) (zv) (zw) (zx) (zy) (zz)

#### DISCUSSION

It is felt that cancellous bone is well adapted for repair of small defects of the skull, especially in the brow region where it is difficult to insert an foreign material such as titanium or acrylic. In view of the superior resistance

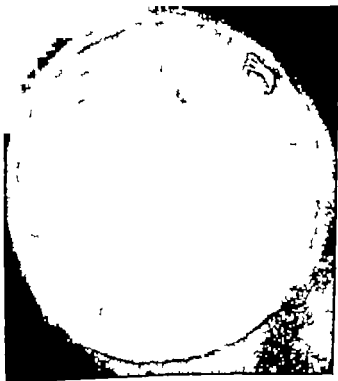


Fig. 1. Patient prior to surgery.

Fig. 2. Patient after surgery.



of cancellous bone to infection, which is always a hazard when working near the nasal sinuses, it is felt to be markedly superior to any foreign material no matter how inert

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# COMPOUND TRANSVERSE FRACTURE OF THE MAXILLA

## REPORT OF A CASE WITH ZYGOMATIC FIXATION

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ACCORDING to Adams, until a few years ago, some type of extraoral appliance was generally employed in cases of severe compound transverse fracture of the maxilla. Since then, however, open reduction and fixation by wiring of the fracture to the neighboring unfractured bone has been performed in most cases. A simple new operative procedure used in the case to be reported, has been devised whereby the floating fracture of the maxilla is attached to the zygomatic arch with tantalum wire. It requires no plaster head caps or cumbersome intraoral or extraoral appliances, and is not uncomfortable for the patient.

### REPORT OF A CASE

M. V. G., an elephanteer, 71 years old man, admitted to the Hospital de la Santa Rosa (Civil Block), on March 6, 1943, with compound transverse fracture of the maxilla. Thirty hours before admission, he had been kicked by a horse the ridge of the horse's hoof striking him directly below the nose producing a comminuted, comminuted, nasal extending through all layers of the upper lip. The bony edges of both upper maxilla were raised. The patient became thus free to see and resting upon the tongue (Figs 1, 2, and 3).

Under intratracheal anesthesia a small drill hole was made in the superior alveolar process just below the former site of the second premolar tooth. A tantalum wire was passed through this hole and the end brought out and over the alveolar ridge. A long, slightly curved, Reverdin needle was then inserted immediately above the anterior end of the gum tissue and pushed down and forward, and axially to enter the mouth at the gingival fold. One end of the wire thus threaded through the needle was brought out superior to the zygomatic arch. The Reverdin needle was then inserted through the same hole in the scalp and passed laterally to the zygomatic arch to enter the mouth at the gingival fold. The second end of the wire was pushed over the alveolar process and then threaded through the Reverdin needle and brought out. The two ends of the wire were then passed through a button 1 cm in diameter. The procedure was performed on the opposite side (Figs 4, 5, and 6). A drill hole was made on each side of the midline of the hard palate 3 mm apart and third wire was passed through these holes and fixed to the buccal perpendicular. Thus the bone ends were not completely separated. The fracture of the left nasal alveolar ridge was elevated and secured in position (Figs 3 and 5). Both maxillary alveolar arches were then pushed with a uniform grade to restore the normal contour of the lips. The soft tissues of the lip were sutured in three layers. The internal wires were then tightened through the button to raise the position of the fracture of the superior maxilla (Figs 4, 5, and 6).

Postoperative care of the patient consisted of a diet of soft and gruel. Follow-up of the operation by x-ray and clinical examination was made every four hours and possible infection was prevented by the use of antibiotics. The first postoperative day (Figs 7 and 8) the patient was able to eat and drink. The patient was discharged through the hospital for eight days.

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James W. M. Internal Wiring Fixation of Facial Fractures.

322-330, 1944

FIG 1



FIG 2

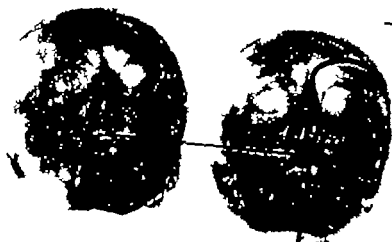


FIG 3





A



B



C

Fig. B and C—Final results 3 years after the operation

Fig. 1. Photograph of patient showing extent of injury.

Line of complete transverse bilateral fracture of the maxilla and displacement of the fracture ends down and displacement of the maxilla after the operation. Note the position of the fracture ends and the position of the maxilla after the operation.



The sutures are removed on the fourth postoperative day. The inflammatory edema subsided by the sixth postoperative day and the patient left the hospital on the fifteenth postoperative day. The wires are removed on the first eighth postoperative day.

The patient made uneventful recovery. If disunion of the fracture has been attained. The patient has now worn his first provisional prosthesis for six years without difficulty. At the age of 43 years he is well looking with no scars.

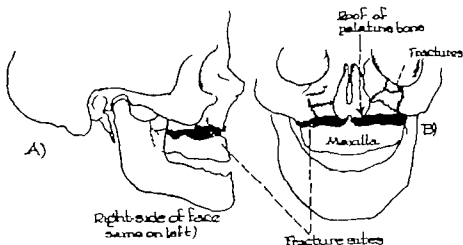


FIG. 1.—Lateral view of fracture site. B from view of fracture site.

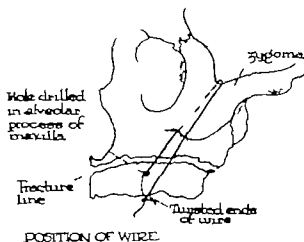


FIG. 2.—POSITION OF WIRE.

FIG. 3.—Position of wire in relation to teeth.

#### COMMENT

This procedure is presented because it is simple to perform and comfortable for the patient. In patients with teeth, the procedure is further simplified by the limitation of the use of drill holes since the teeth may be utilized for fixation of the wires.

## THE EFFECTS OF THE SUPINE POSITION UPON THE VENTILATION OF THE LUNGS OF DOGS

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(From the Department of Physiology, Harvard School of Public Health)

SOME years ago we were struck by the abnormal appearance of lungs of dogs kept under deep anesthesia and held supine for some hours. The lower lobes, dorsally and extending variable distances toward the apices, were congested and liverlike in appearance. It was apparent that blood cells had ceased to move in the capillaries of these dependent parts, though lung edema was not an apparent eventuality so far as we could judge.

A little later Krieger, in 1924, emphasized the role of stasis as a vascular problem, and, as time passed, this conception took more and more hold upon workers in this laboratory. Briefly stated the idea was that in dependent part of the pulmonary circulation in deeply anesthetized dogs, breathing poorly, the blood movement became unduly slow; plasma in small amounts moved out of the capillaries, and the capillary circulation was blocked by packed red cells which lacked plasma to float them along.

In the lungs, the appearance resulting from this phenomenon is a reddish solidity of dependent parts. How serious to a patient such an experience may be is hard to say. As anesthesia passes off and the circulation becomes normally active, it would be our opinion that the stasis of red cells is slowly broken up and normal circulation is re-established.

Many people think of edema as an inevitable result of circulatory block, but this idea is obviously wrong unless blood continues to be forced against a barrier. In the case of stasis, wherever it occurs, the circulation stops, and such small amounts of plasma as may be present in the capillaries of the region may escape. But once this has happened, the area is dry. The production of edema requires an active, or reasonably active supply of blood. It is a progressive process. When the circulation to a part ceases, then only that plasma in the capillaries at the moment can become extravascular, and this is the reason that stasis in pulmonary capillaries does not result in pulmonary edema.

Our first observations were made in the course of other experiments in which dogs anesthetized with nembutal were supine over many hours and entirely immobile. Invariably there was a liverlike solidification of the lower lobes extending up along the spine where lung movement was negligible or absent. When such regions were sectioned with a razor blade they were bloody but the frothy point which one associates with lung edema were absent.

Becoming curious in regard to the situation as it involved the capillaries, we injected intravenously a suspension of fine particles of graphite into dogs, partly in anesthesia, and in others after some hours. These experiments were reported by Drinker<sup>1</sup> in 1945. They showed that when an animal was in the

early stages of anesthesia, graphite particles were widely and uniformly distributed through the lungs but after some hours in the supine position, when the lower lobes posteriorly were red and solid, then injected graphite particles did not enter these areas, indicating blockage of pulmonary capillaries.

The experiments reported in this paper have been designed to discover how far dependent, apparently solid parts of the lungs fail to be reached by air when the animal is breathing normally. It is our belief that the primary condition causing blockage of air entrance into the alveoli is vascular. This conception will be clearer after presentation of experiments and our explanation found in the discussion.

#### EXPERIMENTAL

Under nembutal or sodium veronal anesthesia a tracheal cannula with three openings was introduced, as shown in Fig. 1. This cannula, *E*, enters the trachea of the dog at *F* and two wide ends permit the entrance and exit of aerosol introduced into a bottle *B* by means of a simple atomizer through tube *A*. The bottles used were of 4 liter capacity and into *B* a lead, *C*, delivers a constant stream of oxygen. The stopper *H* in bottle *I* is of loose cotton to avoid the development of pressure and, at the same time, to minimize leakage of the aerosol into the laboratory air.

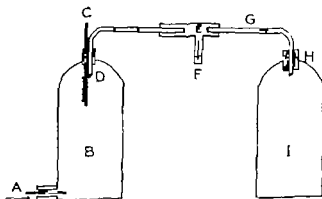


Fig. 1—4, flask from tankcar supplying aerosol; dog serum plus T 1824, 4 liter bottle; *C*, tube for supplying oxygen or oxygen-carbon dioxide mixtures; *D*, tube to tracheal cannula; *E*, entrance of cannula into trachea of dog; *G*, glass tube to room from aerosol bottle; *H*, cotton plug allowing sound and preventing development of pressure in reservoir bottle *I*.

The aerosol employed had the following composition: 200 cc of a 5 per cent solution of T 1824 in 0.85 per cent salt solution added to 300 cc fresh dog serum. The final concentration of T 1824 was thus 0.5 per cent and of dog plasma protein about 3 per cent. The aerosol was made by putting this solution in a bottle and using compressed air to produce the mist. This resulted in a beautiful blue color which was blown into the 4 liter glass bottle *B* from which the dog breathed naturally. The vapors passed into another large reservoir *I* connected with the opposite opening in the cannula and stopped loosely with cotton. This last measure was found necessary and

without it appreciable amounts of the aerosol could be seen in the air of the laboratory and after a number of experiments in which blue was noticed on blowing our noses, some degree of sensitization began to appear and this had to be checked promptly. The reason for adding serum to the dye solution resides in the fact that the addition of protein to T 1-4 solutions prevents the dye from being absorbed from the alveoli, whereas simple water solutions are absorbed at once mainly into the pulmonary capillaries, and distributed promptly all over the body (Drinker and Hardenbergh 194). The addition of the serum anchors the dye aerosol in the alveoli reached by it.

A further interesting fact occurred in the first three experiments. After breathing the aerosol for twenty to thirty minutes, the animal died of anoxia. It was some time before we realized that oxygen under these circumstances was so far replaced by water vapor as to produce inevitable anoxia and death. When oxygen or an oxygen-carbon dioxide mixture was breathed into the trachea through tube (Fig. 1) the difficulty ceased at once.

At the close of each experiment the animal was killed with the trachea was then clamped, and the lungs removed without permitting them to collapse. Colored photographs were made promptly and gave a very graphic picture of the distribution of the blue aerosol which showed not only that half remained open since production of colored illustration is usually expensive. Outline drawings have been made from them and areas blue in color have been typed as seen in Figs. 3, 4 and 5. (Clear remains thus in an part of the lungs where alveoli were not reached by the aerosol.)

A typical experiment was as follows:

Nov. 2, 194	dog weighing 10.2 kilogram
9:30 a.m.	6 cc of per cent nembutal intra-muscul
9:30	1 cc of per cent nembutal intraperitoneal
10:0	5 cc of Ringer solution intravenous
1:00	5 cc of Ringer solution intra-muscul
1:0 p.m.	Animal began to breathe blue aerosol mask described
1:10	5 cc of Ringer solution intra-muscul
2:20	1 cc of per cent nembutal intra-muscul
3:0	5 cc of Ringer solution intra-muscul
3:30	dog bled to death, lungs removed, and colored photograph made twenty five minutes after death

The results of this experiment are shown in Figs. 2 and 3. Fig. 2 shows the posterior aspect of the lungs and it is at once apparent that very little blue has entered the lower lobes except high up. This animal had been immobilized by lack from 9:30 a.m. to 1:0 p.m. and then inhaled the blue aerosol until 3:30 p.m. The result indicates that something over three hours in the supine position causes a considerable degree of alveolar blockage. Fig. 3 is a view of the same lungs from the right side.

Figs. 4 and 5 are again posterior and left lateral view of a dog anesthetized with nembutal and auralpine from 9:30 a.m. to 3:0 p.m. In this case except for a short interval the animal breathed a mixture of 9.46 per cent

early stages of anesthesia, graphite particles were widely and uniformly distributed through the lungs but after some hours in the supine position when the lower lobes posteriorly were red and solid, then injected graphite particles did not enter these areas, indicating blockage of pulmonary capillaries.

The experiments reported in this paper have been designed to discover how far dependent, apparently solid parts of the lungs fail to be reached by air when the animal is breathing normally. It is our belief that the primary condition causing blockage of air entrance into the alveoli is acicular. This conception will be clearer after presentation of experiments and our explanation found in the discussion.

#### EXPERIMENTAL

Under nembutal or sodium veronal anesthesia, a tracheal cannula with three openings was introduced, as shown in Fig. 1. This cannula *E* enters the trachea of the dog at *F* and two wide ends permit the entrance and exit of aerosol introduced into a bottle *B* by means of a simple atomizer through tube *A*. The bottles used were of 4 liter capacity and into *B* a lead, *C* delivers a constant stream of oxygen. The stopper *H* in bottle *I* is of loose cotton to avoid the development of pressure in the same time to minimize leakage of the aerosol into the laboratory air.

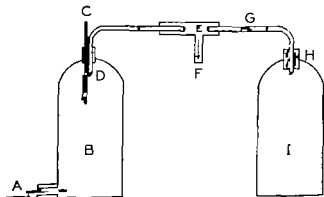


Fig. 1.—A inlet from twister supplying portland dog with gas T 124. B 4 liter bottle. C tube or atomizer for oxygen or oxygen-carbon dioxide mixture. D, line to tracheal cannula. E, F, entrance of cannula into trachea of dog. G, glass tube to remove excess aerosol. H, cotton plug allowing aerosol and preventing development of pressure in reservoir bottle.

The aerosol employed had the following composition: 200 cc of a 1 per cent solution of T 1224 in 0.65 per cent salt solution added to 300 cc fresh dog serum. The final concentration of T 1224 was thus 0.5 per cent and of dog plasma protein about 2 per cent. The aerosol was made by putting the solution in an atomizer and using compressed air to produce the mist. This resulted in a beautiful blue spray which was blown into the 4 lit. glass bottle *B* from which the dog breathed naturally. It was prevented from entering the large reservoir *I* connected with the opposite opening in the cannula and stoppered loosely with cotton. This last measure was found necessary since

without it appreciable amounts of the aerosol could be seen in the air of the laboratory and after a number of experiments in which blue was noticed on blowing our noses, some degree of sensitization began to appear and this had to be checked promptly. The reason for ailing serum to the dye solution resides in the fact that the addition of protein to T 1894 solutions prevents the dye from being absorbed from the alveoli whereas simple water solutions are absorbed at once mainly into the pulmonary capillaries, and distributed promptly all over the body (Drinker and Hardenbergh, 1947). The addition of the serum anchors the dye aerosol in the alveoli reached by it.

A further interesting fact occurred in the first three experiments. After breathing the aerosol for twenty to thirty minutes, the animal died of anoxia. It was some time before we realized that oxygen under these circumstances was so far replaced by water vapor as to produce inevitable anoxia and death. When oxygen or an oxygen-carbon dioxide mixture was bled into the system through tube C (Fig. 1) the difficulty ceased at once.

At the close of each experiment the animal was bled to death, the trachea was then clamped, and the lungs removed without permitting them to collapse. Colored photographs were made promptly and gave a very graphic picture of the distribution of the blue aerosol which obviously entered alveoli that had remained open. Since reproduction of colored illustrations is unduly expensive, outline drawings have been made from them and areas blue colored have been stippled as seen in Figs. 2, 3, 4 and 5. Clear regions thus mean parts of the lungs where alveoli were not reached by the aerosol.

A typical experiment was as follows:

Nov. 1, 1945	dog weighing 10 kilograms
9:30 AM	6 cc of 5 per cent nembutal intravenously
9:30	3 cc of per cent nembutal intraperitoneally
10:0	50 cc of Ringer's solution, intravenously
10:00	50 cc of Ringer's solution intravenously
10 PM	Animal began to breathe blue aerosol, nasal cannula described
1:10	50 cc of Ringer's solution intravenously
2:20	1 cc of per cent nembutal intravenously
3:00	50 cc of Ringer's solution intravenously
3:50	Dog bled to death, lungs removed, and colored photographs made twenty five minutes after death

The results of this experiment are shown in Figs. 2 and 3. Fig. 2 shows the posterior aspect of the lungs, and it is at once apparent that very little blue has entered the lower lobes except high up. The animal had been immobile on his back from 9:30 AM to 10:00 PM and then inhaled the blue aerosol until 3:00 PM. The result indicates that something over three hours in the supine position causes a considerable degree of alveolar blockage. Fig. 3 is a view of the same lungs from the right side.

Figs. 4 and 5 are again posterior and lateral views of a dog anesthetized with nembutal and supine from 9:00 AM to 3:00 PM. In this case except for two short intervals the animal breathed a mixture of 94.6 per cent

early stages of anesthesia, graphite particles were widely and uniformly distributed through the lungs but after some hours in the supine position, when the lower lobes posteriorly were red and solid, then injected graphite particles did not enter these areas, indicating blockage of pulmonary capillaries.

The experiments reported in this paper have been designed to discover how far dependent, apparently solid parts of the lungs fail to be reached by air when the animal is breathing normally. It is our belief that the primary condition causing blockage of an entrance into the alveoli is vascular. This conception will be clearer after presentation of experiments and our explanation found in the discussion.

#### EXPERIMENTAL

Under nembutal or sodium veronal anesthesia, a tracheal cannula with three openings was introduced as shown in Fig. 1. This cannula *E* enters the trachea of the dog at *P* and two side ends permit the entrance and exit of aerosol introduced into a bottle *B* by means of a simple atomizer through tube *A*. The bottles used were of 4 liter capacity and in *B* a lead, *C* delivers a constant stream of oxygen. The stopper *H* in bottle *I* is of loose cotton to avoid the loss of pressure but at the same time to minimize leakage of the aerosol into the laboratory air.

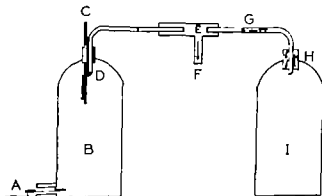


Fig. 1. *B*, 4 liter glass bottle used to introduce aerosol into trachea of dog. *I*, 4 liter glass bottle used to receive aerosol from trachea of dog.

The aerosol employed had the following composition: 200 cc of a 1 per cent solution of T 1824; 0.85 per cent salt solution added to 300 cc of fresh dog serum. The final concentration of T 1824 was thus 0.6 per cent and of dog plasma protein about 3 per cent. The aerosol was made by putting this solution in an atomizer and using compressed air to produce the mist. This resulted in a beautiful blue vapor which was blown into the 4 liter glass bottle *B* from which the dog breathed naturally. Excess vapor passed into another large reservoir *I* connected with the opposite opening of the cannula and stoppered loosely with cotton. This last measure was found necessary and

but was slower than one is accustomed to seeing when using such mixtures. The results indicate marked failure of the aerosol to reach the posterior parts of the lower lobes. Possibly a more vigorous response to the carbon dioxide would have lessened this effect but the fact remains that even with a fair degree of increased breathing, alveoli in these dependent and relatively immobile areas are not reached by the aerosol.

# DISCUSSION AND CONCLUSIONS

This paper concentrates upon the failure of air to enter alveoli in certain parts of the lungs placed at a disadvantage as a result of prolonged fixation in what for the dog is certainly an abnormal position. Dogs do not sleep or rest flat upon the back. But it is equally true that except under anesthesia or as a result of injury man does not remain in a fixed position during sleep. In sleep he moves frequently with the result that stasis in the pulmonary capillaries in any one region is ailed. In experiments through many years, invariably whether upon anesthetized dogs or other animals apparently in the best of health lung conditions like those we have described have been seen repeatedly. Their significance when applied to prolonged surgical operations in man cannot be estimated other than to point out that after long anesthesia every patient is left with a circulation and ventilation of the lungs which are not normal and must be corrected before the patient is in normal health once more. That these blocked pulmonary capillaries begin again to transmit blood when healthy animals recover from anesthesia and begin to move about is certainly the case. But in old and feeble persons reluctant to cooperate and stoutly opposed to being moved or bothered in any way it is not easy to accomplish changes in position which may ward off serious complications in the lungs. It was our idea that occasional periods of inhalation of 93 per cent oxygen and 7 per cent carbon dioxide might be an easy method of avoiding atelectasis. This is by no means certain unless the anesthesia is short and the periods of inhalation are begun early in the operation.

It is natural to ask why healthy anesthetized dogs, kept in one position and quite immobile, experience stasis in certain pulmonary capillaries, accompanied by blocking off of alveoli and atelectasis. As has been pointed out the supine position is an unusual one for the dog and, lacking anesthesia, never maintained except for short periods. When a man in these experiments, the animal is upon an inclined table for some hours the dorsal and dependent parts of the lungs are pressed against the posterior part of the thorax which in turn is supported by a rigid animal board. The movement under these conditions is in the sternal part of the chest which is the free part. Under normal circumstances the lungs sit in a large amount of blood in a meshwork of interconnecting capillaries. With a relatively slow blood flow all that is necessary to make back just a generation of the blood, there is settling of blood in the dependent part of the lungs which lie against the most rigid part of the chest. In our opinion this settling coupled with little movement of the alveoli, overfill the capillaries and after a time there is blockage of flow with leakage of a



carbon dioxide and 80.54 per cent oxygen. The aerosol was breathed from 1.30 p.m. to 3.20 p.m. and was produced by the usual blast of compressed air. During this time the oxygen-carbon dioxide mixture was blown into bottle A through tube C. Breathing in the carbon dioxide a deeper than normal

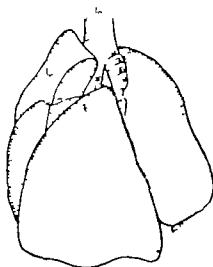


FIG. 3

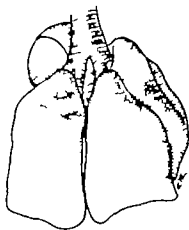
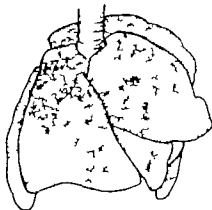


Fig. 2

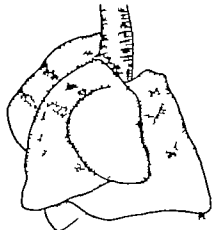


FIG. 1

Fig. 3.—Posterior view of lungs of dog, which inhaled oxygen and aerosol T 82 aerosol for 2 hours. At 12 minutes after 2 hours and 15 minutes in supine position under anaesthetic aethers. The areas covered by black dots indicate those reached by the aerosol.

Fig. 2.—Right lateral view of lungs from dog. Fig.

Fig. 4.—Posterior view of lungs of dog, which inhaled carbon dioxide and aerosol T 122 aerosol for 2 hours and 25 minutes after lying supine for 2 hours and 15 minutes under anaesthetic 10 minutes. The areas covered by black dots are those reached by the aerosol.

Fig. 1.—Left lateral view of lungs from dog in Fig.

### POSTERIOR CISTERNAL DRAINAGE OF THE HYDROCEPHALIC THIRD VENTRICLE (POSTERIOR THIRD VENTRICULOSTOMY)

small amount of plasma into the alveoli and possible eventual blockage of bronchioles. Dock and Harrison, in 1944 related bed rest to the development of pulmonary complications in bedridden patients, particularly those with cardiac disease. In the case of healthy dogs under barbiturate anesthesia, it is probable that cardiac output was reduced as compared with the unanesthetized state and this factor would of itself tend to promote stasis and alveolar collapse. The same localization of stasis to the sternal margins of the lungs with subsequent alveolar collapse can be made to occur along these margins of the lungs if the anesthetized dog is placed prone instead of supine.

## SUMMARY

1 The development of stasis and blockage of pulmonary capillaries in dogs anesthetized with barbiturates and held supine for some hours is described.

The effect of this stasis, which occurs essentially in dorsal and dependent parts of the lungs, is to bring about slight transudation of plasma into the alveoli with blockage of air entrance. Atelectasis slowly develops.

3 Much experience has shown that normal dogs so treated and allowed to recover from the anesthetic (nembutal) usually show no signs of trouble from the lung condition which must have been present when anesthesia terminated and consciousness returned. This does not preclude the fact that in every case of prolonged anesthesia or immobilization in single position the animal or man so treated must dispose of an abnormal pulmonary condition before normal health is attained.

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of primary or atypical amyloidosis, and as such it always has been associated with amyloidosis in other sites such as the heart, gastrointestinal tract and spleen.\* Weismann, Clagett and McDonald found reports of three cases of localized amyloid disease of the lung and added a fourth case of their own.

We wish to report a case of amyloidosis in which the amyloid material formed a single tumor which caused obliteration of a bronchus of the right lung and collapse of the adjacent pulmonary tissue.

#### CASE REPORT

A retired man, aged 60 years, had been an executive for telephone company as referred to the hospital on Nov. 1, 1946 for treatment of tumor of the right lung. Three months before the patient came to the hospital he had had a mild cerebral vascular accident but he had recovered promptly and completely. At the time of this illness the systolic blood pressure had been 200 mm. of mercury but it had gradually decreased to 140 mm. as a result of treatment.

Seven weeks before the patient came to the hospital he had noted for the first time burning or lacerative sensation in the course of exercise. The pain or sensation was not associated with the ingestion of food; it did not radiate and it was relieved by rest. In subsequent weeks, this sensation seemed to be induced by lesser degrees of exertion and because he came to the hospital it could be elicited by his walking to work. A cough productive of minimal quantity of sputum, had been noted about a week previously. The sputum never had been bloody. An incident of mild shortness of breath had appeared 3 days before presentation to the hospital. In the two weeks before the patient entered the hospital his weight had declined from 154 to 144 pounds (69.9 to 64.4 kilograms).

Three weeks before he came to the hospital roentgenographic examination of the thorax had disclosed a mass of the right lung. Electrocardiogram and roentgenograms of the stomach and colon had not revealed any abnormalities.

When the patient was examined at the hospital he was rather ill-nourished and did not appear to be in distress. The systolic blood pressure was 145 mm. of mercury and the diastolic pressure was 90 mm. The pulse rate was 96, and the oral temperature was 99.4° F. Physical examination of the thorax did not disclose any abnormality. The right lung gland was slightly enlarged and described nodules. A fine tremor of the hands was discovered. The result of the remainder of the physical examination was essentially negative.

The blood and urine were approximately normal and the result of a flocculation test for syphilis was negative. Roentgenographic examination of the thorax revealed an obstructive lesion of the bronchus of the middle lobe of the right lung and atelectasis of the lobe. On Nov. 25, 1946, the basal metastatic rate was 30 per cent. The administration of compound solution of salicylic acid in doses of 10 minims (0.6 ml.) three times a day was begun. On December 12, the basal metastatic rate was 35 per cent.

Bronchoscopy was performed on December 13 and it disclosed tumor mass in the bronchus of the middle lobe of the right lung. Mucous pur examination of secretions obtained from the bronchus did not disclose any neoplastic cells. On December 14, bronchography disclosed filling defect of the lumen of the middle lobe.

The resection was performed on December 16. The removed portion of the thoracic gland gland. Gross and histological single degenerating adenocarcinoma. Subsequently the basal metastatic rate decreased as follows: 1 per cent on Dec. 14, 15, 16. At that time he began compound solution of salicylic acid as reduced 3 minims daily.

On Jan. 1, the right side of the thorax exposed by making posterolateral incision and removing a portion of the sixth rib. A large red tumor mass of the middle lobe of the right lung, and it was not in the middle lobe. The tumor was completely removed. The mass had filled the bronchus of the middle lobe of the right lung. The malignant lesion therefore the right lung was removed and the right pharynx was interrupted completely. A tracheostomy of the trachea and the basal metastatic rate decreased to the course of the operation.

## Case Reports

### TUMOR FORMING AMYLOIDOSIS OF THE LUNG

#### REPORT OF CASE

ALLAN L. HANLEY, M.D., O. THURMOND CLAGGATT, M.D.† AND  
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**A**MYLOID deposits have been encountered in many parts of the body. The most familiar manifestation of amyloidosis is the extensive deposition of amyloid in organs such as the liver, kidneys, and spleen in the course of chronic suppurative disease. There have been increasingly frequent observations of amyloid in other organs either with or without preceding disease; consequently amyloidosis has been divided into the following four types according to the classification of Reimann, Konecny, and Ekland: (1) primary amyloidosis (systemic or atypical amyloidosis) which usually involves multiple sites in the mesodermal tissues such as heart, lungs, and skeletal muscle and usually is unaccompanied by antecedent disease; (2) secondary amyloidosis, which is characterized by deposition of the substance in the liver, kidneys, and suprarenal glands in the late stages of chronic suppurative disease; (3) tumor-forming amyloidosis, which is characterized by the formation of solid tumors usually in mesodermal tissues and commonly without antecedent disease as a possible etiologic factor; and (4) amyloidosis associated with multiple myeloma in such sites as lymphoid tissue, bone marrow, and in or around the joints.

The localization of the deposit of amyloid is by no means as sharply delimited as this classification would indicate; moreover, the association with previous disease is so inconsistent that many instances of the disease cannot be placed in either of the first two categories. Tumor-forming amyloidosis is generally regarded as a type of primary or typical amyloidosis. An extensive consideration of the types of amyloid disease and of the surgical significance of localized amyloid deposits was presented recently by Wismann, Claggett, and McDonald.

Tumor-forming amyloidosis has been observed in several parts of the body; among them the skin, tongue, larynx and trachea, urinary bladder, and urethra. According to Fligman, when amyloidosis occurs in the upper part of the respiratory tract the sites of involvement in order of decreasing frequency are the larynx, trachea, and pharynx. Up to 1944 six cases of amyloid tumors of the urinary bladder had been reported in the literature. In these organs and in other sites, the amyloid tumors have occurred as small, well-circumscribed masses lying in the subepithelial stroma. In the lungs, amyloidosis has occurred in the form

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of cells remained. The involved blood vessels were usually of small caliber; in some instances the wall of these vessels were one or two times as thick as normal. Throughout the rest of the tumor there were many giant cells which had pinkish cytoplasm and from 8 to twenty nuclei.

In sections stained with crystal and methyl violet (Fig. 3) the homogeneous material was stained reddish violet, which is characteristic of amyloid. This reaction is particularly noticeable around blood vessels. The entire tumor is stained characteristically with methyl violet. In these sections, the deposition of the amyloid in the interalveolar septa is more extensive than is apparent in the sections that had been stained with hematoxylin and eosin. There was deposition of calcium throughout the tumor mass.

In other sections that were stained with an Orison connective tissue stain, the variable staining reaction of the amyloid in different parts of the tumor was evident. The amyloid in the center of the larger masses was stained yellow green while that lying at the periphery of these masses was stained dull red. The dull red color of the amyloid was due to the fact that from the brilliant red of collagen in the sections.



Fig. 3.—The amyloid is deposited in interalveolar septa and in the walls of blood vessels. The dense black material is amyloid stained with crystal and methyl violet. Some of the adjacent normal lung tissue is visible. (X100)

The distribution of amyloid was somewhat irregular regardless of the staining method that was used. The best of all amyloid stains depends on the method of fixation used in the alveoli. The alveoli had been compressed to a certain degree and the reaction of the amyloid was somewhat irregular. The alveoli had been compressed to a certain degree and the reaction of the amyloid was somewhat irregular. The alveoli had been compressed to a certain degree and the reaction of the amyloid was somewhat irregular.

Having been stained with the Orison connective tissue stain, the amyloid in the center of the larger masses was stained yellow green while that lying at the periphery of these masses was stained dull red. The dull red color of the amyloid was due to the fact that from the brilliant red of collagen in the sections.

#### DISCUSSION

The case which has been reported here has been accepted as an example of primary tumor of the lung in the following grounds. There was no history of previous neoplasia. The tumor was of the type commonly encountered

Pathologic examination of the right lung disclosed a very hard mass 8 cm in diameter in the middle lobe (Fig. 1). The tumor was mottled gray and black in color and it was firmly embedded in the surrounding lung tissue. The bronchus of the middle lobe passed directly into the mass and was completely occluded by it. It was impossible to pass a small probe into the bronchus within the tumor. The tissue of the middle lobe round this mass was completely collapsed; the lobe was about one half its normal size. Microscopic examination of fresh frozen sections of the mass that had been stained with polychrome methylene blue disclosed dense infiltration of homogeneous black material the walls of blood vessels, alveoli and bronchi.



Fig. 1.—Aneurotic mass in the middle lobe of the lung surrounding and occluding the middle lobe bronchus near its origin. The adjacent tissue of the middle lobe is (brown and reduced in volume).

Sections that had been fixed in alcohol and stained with hematoxylin and eosin showed extensive deposition of homogeneous pink staining material which seemed to be laid down primarily in the walls of small blood vessels and in the interalveolar septa. In lesser extent, the material was seen in the walls of bronchi around the bronchial cartilages and mucous glands. In places it could be seen that the material had been deposited concentrically around blood vessels and alveoli and some adjacent vessels had become occluded. At some points, the alveoli were fairly well preserved and easily recognizable as such. At other points, even the center of larger vessels the alveoli had been so compressed that only clumps

# Surgical Technique

## CONGENITAL MACROGLOSSIA

### REPORT OF TWO CASES

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ALTHOUGH a variety of inflammatory and neoplastic processes will increase the size of the tongue in part or in whole, the term *macroglossia* has come to be reserved for two distinct entities. One is a lymphangiomatous enlargement and the other a true hypertrophy of the lingual musculature.

Embryologically the tongue develops in two parts, the buccal and the pharyngeal. These differ in origin, development, structure and function and are separated by a V shaped groove, the sulcus terminalis. Our knowledge of the development of the tongue contributes little to our understanding of the etiology of either form of macroglossia. Haag and Waldajfel, however, have commented on the foetal development of lymphangiomatous growth at the line of union between the anterior and posterior part of the tongue as lending significant support to the theory of their embryonal origin.

*True muscular macroglossia* is a congenital hypertrophy of the muscle fibers of the tongue. It may or may not be associated with localized or generalized muscular hypertrophy elsewhere in the body. It is rarely found free from other congenital abnormalities. It is usually associated with cretinism, mongolism and choledyl. The gross pathological picture may be one of localized muscular hypertrophy, of partial enlargement or a uniform muscular growth of the whole tongue. Bostein and associates have suggested a practical classification dividing muscular macroglossia into four clinical types. Microscopically there is a definite increase in the diameter of the muscle fibers. Surgery with partial removal has been the treatment of choice in this type (Bassetta, Welzel and Lengemann). Recently, however, Abelson and associates have questioned the advisability of surgical removal and they have reported a case of spontaneous resolution of true muscular macroglossia.

Lymphangioma is by far the most common cause of macroglossia. This was asserted originally by Virchow. Bassetta and other writers. It has been suggested that a congenital rest which produces new lymphatics or the congenital absence of afferent lymph vessels, may be an etiologic factor in lymphangiomatous enlargement. The presence of innumerable lymph vessels, perhaps due to dilatation in subsequent infection with resultant obstruction and dilatation of the lymphatics, has been proposed as a basis of error.

Lymphangioma may manifest itself as a localized nodule in the tongue or as a diffuse enlargement of the whole organ. The protruding tongue usually becomes fissured and clefted. Infection or ulceration resulting in necrotic ulcers



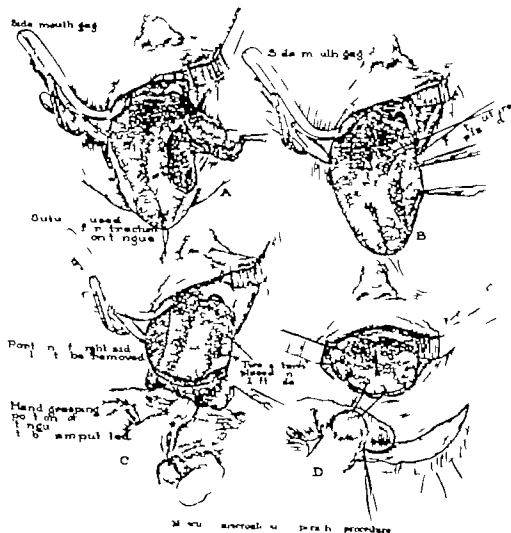
in secondary amyloidosis. Although it is impossible to say with certainty that there was not amyloidosis of other mesodermal tissues as seen in cases of diffuse or systemic primary amyloidosis, there was no evidence from the history or physical examination that such involvement existed. The staining reactions with the special stains employed have been accepted as dependable evidence that the tumor was composed of amyloid.

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associated with lymphangioma of the neck the so-called cystic hygroma. Little reported this association in three cases. The tongue, the floor of the mouth, and the suprathyoid region may all be involved.

Surgery is indicated in this condition. A wedge-shaped incision is made preferably by cauterization. The tongue is reshaped as close to normal as possible. Postoperatively the maintenance of an adequate airway and the control of oral sepsis are prime considerations. Frequently a secondary resection is necessary. Radiation therapy, although frequently resorted to, offers little help in this



This patient has a peripheral sublingual lymphangioma. What is the best treatment? The answer is: a wedge-shaped resection of the tongue and floor of the mouth.

Biopsy and histology examination are necessary to establish the diagnosis. The resection of the tongue and floor of the mouth is necessary.

further obstruction and progressive enlargement. Microscopically one sees replacement of muscle by lacunae containing scattered fixed blood cells, constituting a vast lymph vessel tumor. Vessels on the surface are filled with blood from ruptured adjacent capillaries. The lymph spaces are enlarged and small hemangioma like areas are produced. Lymphangiomatous macroglossia is frequently



FIG. 1 (Case 1).—A, 4 months preoperative; B, 10 months; C, 1 year 6 months; D, 2 years 6 months. (A, B, C, D, 1922.)

The family history was noncontributory. The mother, as 36 years old and the father died an accidental death at the same age. On making 7 year old boy was in good health like no abnormalities. One other pregnancy had resulted in miscarriage at week before term.

The child was breast fed. She seemed mentally deficient during the first few months but later gave no evidence of maldevelopment. The inferior teeth were present at 6 months of age and all teeth except the upper molars at 12 months. She talked at 15 months and was speaking short sentences at 27 months of age.

On physical examination in January 1930, when 7 months of age she weighed 10 kilograms. The tongue was enlarged to four or five times the normal size, completely filled the mouth, and protruded beyond the lips at all times except on swallowing. It did not taper at the tip but was bluntly rounded. The surface showed smooth uninterrupted



Fig. 1. (A) Frontal view of young child. (B) Profile view of young child. (C) Frontal view of older child. (D) Profile view of older child.

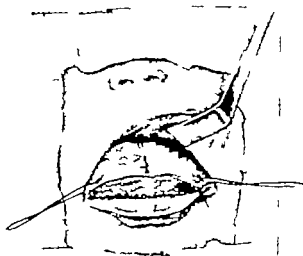
## CASE REPORTS

We wish to report on the patient with uniform enlargement of the tongue seen in the surgical service of the University of California Hospital.

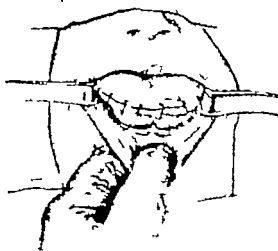
CASE 1—E. A. B., girl, born five weeks prematurely of polyhydramniotic mother had macroglossia and an unilateral hernia at birth. The hernia surgically corrected at the time.



Fig. 1 (Case 1)—Macroglossia. A, Surgical specimen the tip and lateral edges of the tongue. B, simple anastomosis hypertrophy. C, dense and relaxed bundles of striated muscle.



A



B

Fig. 1. A. Diagram of the jaw with a large, rounded, protruding mass. B. Diagram of the jaw with a large, rounded, protruding mass.

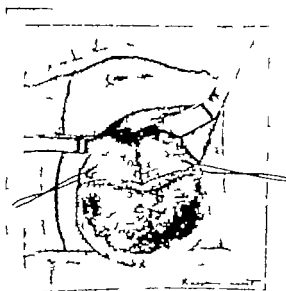


Fig. 1, B, C and D—Laryngotracheal osteoplastic operation procedure





epithelium. The mandible projected forward (prognathism) and x-ray examination showed shortening of the horizontal ramus. The lower incisor teeth are pointing anteriorly from buccal pressure. A small sublabial scar is present. Laboratory studies are not remarkable.

**Operation.**—The lateral edges of the gum tissue were removed, each extending to the portion of the tip of the tongue. In all, three pieces, eaching 12 cm were excised (Fig 1).

**Microscopic examination** shows simple nodular hypertrophy with loosely arranged interlacing bundles of striated muscle. Endothelial cells are not increased. The arterioles are normal.

**Subsequent Course.**—The child returned to the hospital in 1937 for removal of an adenoma of the frenulum of the tongue which restricting its movement. The teeth are straight and the jaw relation is improved. In February 1939, at 4 years of age the teeth were in normal position. The tongue much smaller than when she was last seen. She talked well and had difficulty only when she was very excited. Her next visit was not until ten months later (October 1940) when no signs of defect were noted. Her speech and development normal had been within limits.

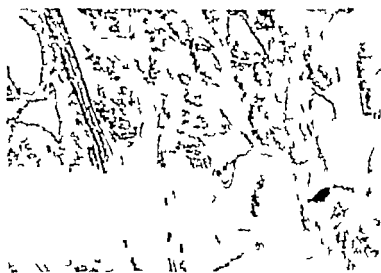


Fig 1 (Case 1).—*Leptothorax* *maculatus*. The histological picture is typical of the disease. The tissue is composed of spindle-shaped cells, some of which are arranged in bundles.

**Case 2.**—A girl, as born in 1944, full term and of normal weight with birth weight of 7 pounds. At birth the tongue is slightly enlarged, all small hemangiomas like areas along the periphery of the tongue. The skin is present in the sublabial area of the neck. There are no other lesions. The overlying skin is normal. The hemangiomas are not increased.

The family history is unremarkable. The mother and father are both 39 years old and in good health. There are seven children, four boys and three girls, all of whom are well.

The baby had frequent vomiting and diarrhea, and in May, 1944, she was taken to the hospital. At that time, five months after birth, the tongue began to enlarge rapidly. It increased in size three times the normal size and blood began to appear from the hemangioma-like areas of the tongue.

Development otherwise was normal. She sat down and had the first tooth at 7 months of age, talked at 15 months, walked at 16 months, and had bladder and bowel control by

yield, on injury a sufficient amount of fat to cause lipemia and embolism. Fractures of the tibia and femur are the most frequent causes of fat embolism. Seriba<sup>1</sup> calculated the amount of fat present in the average adult femur to be 71 gm. In studies relating to experimental fat embolism he calculated that the femur of a dog weighing 14 kilograms contains on the average 127 gm. of fat while the femur of a rabbit weighing 4 kilograms contains an average of 13 gm. of fat.

Of the numerous accounts of fat embolism of the lung, brain and kidney following fracture only occasional reference is made in the literature to the occurrence of embolic phenomena in the capillaries of the gastrointestinal tract. Seriba, in 1879 noted fatty emboli with capillary hemorrhage in the mucosa of the stomach and intestine. LeCount and Gauss noted fat emboli in the vessels of the gastric mucosa in some of their fourteen cases of fat embolism associated with fractures at autopsy. Warthin stated that there is not a single organ or tissue in the body that does not get some fat in its capillaries during a fatty embolism and he has found emboli of fat to occur in the capillaries of the stomach and intestine.

Furthermore the only allusion to the occurrence of gastrointestinal erosion and/or ulcer following fracture other than that made by one of us (O. H. W.) in 1945 is to be found in a discussion of a paper by Sternberg in 1907. Schridde, in this discussion stated that he had twice observed fat embolism at post mortem in the submucosal gastric arteries accompanying fracture. In one patient a 70-year-old man, there were numerous erosions and twenty superficial ulcers. The patient died of coma which had persisted following the fracture. Schmorl in a six line discussion at the same meeting of the German Pathological Society stated that he too had observed punctate hemorrhages in the gastric mucosa due to fat embolism following fractures and severe bodily contusions. Vale and Cameron, in a paper concerning the occurrence of gastric and duodenal perforation during hospital treatment reported a case of a 54-year-old man who being struck by an automobile sustained a fracture of the right clavicle and a compound fracture of the right leg. Twenty-one days after injury and treatment of the fractures, and while on a regimen of bed rest and a soft diet, the patient developed a perforated duodenal ulcer which was surgically closed. They stated that trauma sustained at the time of injury may be mentioned as a possible causative factor.

Gastrointestinal bleeding on a psychic or emotional basis following minor surgical procedures in four cases was reported by Brooke. Herbert observed in a patient who developed acute peptic ulcers following llistant peritonitis. He stated that the causes of the ulcers were not apparent.

Experimentally Magenli<sup>2</sup> during the years 1881 to 1896 before the occurrence of pathologic fat embolism in man was known performed many experiments upon animals to determine the effect of the injection of oil into the circulating blood, and discovered that the fluid fat would not pass the smaller vessels, but blocked them mechanically. Lister in 1869 had injected large amount of milk intra-venously into dogs. Seriba (1899) pointed out that a drop of fat could pass through the lungs without difficulty. Lehman and

# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## THE RELATIONSHIP OF BONE TRAUMA TO THE DEVELOPMENT OF ACUTE GASTRODUODENAL LESIONS IN EXPERIMENTAL ANIMALS AND IN MAN

WITH PARTICULAR REFERENCE TO THE ROLE OF FAT EMBOLI

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### HISTORICAL

THE occurrence of fat embolism following trauma in man was first recognized in 1889 by Zenker who described a case of fat embolism of the pulmonary capillaries in a laborer who died following a crush injury with multiple fractures of the ribs. That fat embolism in the lung and local as common occurrences in patients dying early after fracture of long bones is well known. Warthin in an extensive review of the literature in 1913 stated that, it is highly probable that in every case of amputation or fracture of the long bones some fat is set free from the ruptured fat cells and enters the blood stream to cause fat-embolism in the pulmonary capillaries, or passing the lungs, in the capillaries of some other organ. The gravity of the condition will depend upon the anatomical importance of the passages blocked by the fat-emboli. He reported, in addition twelve cases of fat embolism, out of a relatively small post mortem series of 600 autopsies, nine of the twelve following fracture of the long bones. Of the five cases terminating fatally post mortem examination in all showed a marked fatty embolism as the cause of death.

Warthin stated that the mechanism of fat embolism following fracture is a release of liquid fat from the marrow of the fracture site which gains entrance into the vascular system by virtue of increased tension at the site of injury forcing the fat into the openings of the bone. In addition, there is entrance of free fat into the lymphatics thus occurs later than the direct entrance of fat into the circulation. The fat then enters the thoracic duct and then passes through the venous circulation into the lungs, constituting a second supply of fat to reach the lungs.

Fat embolism of clinical importance occurs most commonly following fractures of the bones containing fatty marrow. Less frequently it is caused by injury to adipose tissue. Osteoporotic bones in old people or in young individuals who possess atrophic bones from disuse are especially likely to

This study is supported in part by the United States Public Health Service (Lester B. Research) the Augustus L. Reeser Fund, the Donald P. and Mrs. M. W. Reeser Fund, and grants from the National Cancer Institute.

In the four remaining cases definite erosions and petechial bleeding points were noted in the stomach and duodenum. The age of the patients ranged from 17 to 93 years, the majority being about . . . . . The time of death after fracture varied from one to eighty three days, death occurring within three weeks from the time of fracture in all but five cases. Hemorrhage from the gastrointestinal tract, recognized clinically and recorded as hematemesis or melena, was observed in twelve of the twenty nine cases tabulated. In five additional instances autopsy revealed evidence of bleeding not recognized clinically. Ureter therapy was instituted in seven cases diagnosed clinically; two of these patients recovered completely. One patient (L. W. Hospital No. 70487) a 36-year-old man, having sustained multiple fresh fractures in an automobile accident was admitted to the University Hospital on Dec. 10, 1940. Fat was demonstrated in

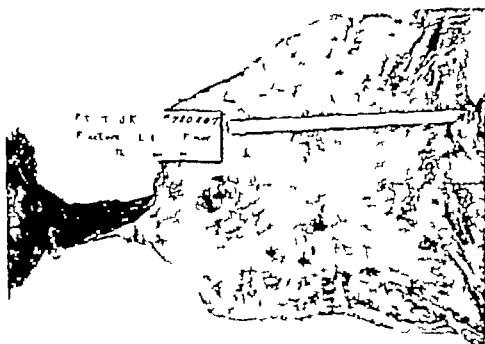


Fig. 1—Stomach  
No. 70487) and  
on Aug. 2, 1941  
hemorrhage occurred  
and the patient died on the eighth hospital day.

(Hospital  
No. 70487  
on Aug. 2, 1941  
hemorrhage occurred  
and the patient died on the eighth hospital day.)

the urine of the patient the day following admission but no abnormal lipemia was observed. He suffered one episode of dyspnea. On the twenty-second hospital day hematemesis occurred followed by melena, which continued for one week, necessitating blood transfusions. The prothrombin time and vitamin C level in the blood were normal. The patient eventually made a satisfactory recovery and was dismissed to his physician. There had been no antecedent story of ulcer or bleeding. Another patient (L. N. Hospital No. 15585) a 66-year-old man was admitted to the University Hospital on March 27, 1940. Melena occurred thirty-five days after a fresh fracture of the neck of the right



In the four remaining cases definite erosions and petechial bleeding points were noted in the stomach and duodenum. The age of the patients ranged from 14 to 93 years, the majority being about 50. The time of death after fracture varied from one to eighty-three days, death occurring within three weeks from the time of fracture in all but five cases. Hemorrhage in the gastrointestinal tract, recognized clinically and recorded as hematemesis or melena was observed in twelve of the twenty-nine cases tabulated. In five additional instances autopsy revealed evidence of bleeding not recognized clinically. Ulcer therapy was instituted in seven cases diagnosed clinically; two of these patients recovered completely. One patient (I. W. Hospital No. 6774) a 36-year-old man, having sustained multiple fresh fractures in an automobile accident was admitted to the University Hospital on Dec. 10, 1940. It was demonstrated in

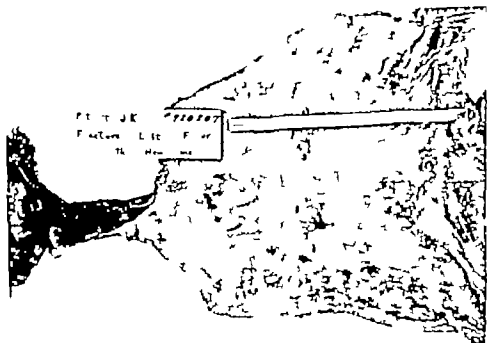


Fig. 1—Stomach

the urine of the patient the lack of flowing a hourson but normal lipemia was observed. He suffered one episode of lipemia. On the twenty-second hospital day hematemesis occurred followed by melena, which continued for one week, necessitating blood transfusion. The prothrombin time and vitamin C level in the blood were normal. The patient eventually made satisfactory recovery and was dismissed to his phisician. There had been no antecedent signs of ulcer or bleeding. Another patient (I. N. Hospital No. 18885) a 69-year-old man was admitted to the University Hospital on March 1, 1942. Melena occurred thirty-five days after a fresh fracture of the neck of the right

Moore in 1927 presented experimental evidence suggesting a nontraumatic origin of fat embolism—the source of fat being the ultramicroscopic emulsion of fat in the normal blood plasma which may form fat droplet of emboli due to physical or chemical alterations in the blood. Virchow<sup>12</sup> in 1862 showed that the experimental injection of minutely emulsified fat was not followed by embolism. He was one of the first to foster the theory of vascular blocking in the genesis of peptic ulcer—a deduction which Virchow made from observing the funnel-shaped character of many ulcers.

#### PRESENT STUDY

Experimental studies concerning the relationship of fracture of long bones to gastroduodenal pathology have been reported in abstract form from this clinic previously.<sup>13-15</sup> The studies have been enlarged upon. This presentation embodies a series of studies concerning the relative incidence of acute gastroduodenal ulcer and/or erosions complicating fractures and amputations of long bones in patients dying early after fracture or amputation and submitted to necropsy as well as in patients who recovered following fracture. In addition, experimental evidence is presented concerning the occurrence of simula gastroduodenal lesions in animal subjected to operative fracture or intravenous administration of nonemulsified fat.

#### A STUDY OF THE INCIDENCE OF GASTRODUODENAL ULCER AND/OR EROSION COMPLICATING FRACTURE OF LONG BONES IN MAN

The observation of a few cases of hematemesis from erosion or ulcer complicating fracture of bones in man, reported in 1945<sup>16</sup> prompted a review of the records from the files of the Department of Pathology of the University of Minnesota concerning fractures in patients coming to autopsy. Over a period of time extending from 1920 to August, 1947 there were 1,432 autopsies performed on individuals who died following fractures of bones, excluding skull fractures. The etiologic factor involved in the occurrence of peptic ulcer in head trauma may be complex, particularly as Cushing<sup>17</sup> has suggested, if the diencephalon is involved. Also those cases in which there was a question of post mortem autolysis of tissues or evidence of chronicity of the ulcers, clinically or pathologically, were not included in the study.

In a series of 1,000 consecutive autopsies of patients dying of all causes, it was noted by one of us (F.B.M.) that of the patient demonstrated gastroduodenal ulceration, eight of whom died of peptic ulcer per se and its complications. Thus, thirty-two patients presented coincidental gastroduodenal ulceration (acute and chronic, but excluding healed scars of ulcers); however in six of these cases it was not possible to rule out enteral changes due to autolysis and post-mortem digestion. The incidence of coincidental acute and chronic ulcers, then, is between 6 and 3 per cent among routine autopsies.

Twenty-seven cases, demonstrating either typical acute or subacute ulceration or erosion of the stomach and/or duodenum following fracture are listed in Table I. In addition, two cases with recovery are appended. It is to be noted in this tabulation that 13 of the 27 cases presented at autopsy definite ulceration (eight gastric, fourteen duodenal and one both gastric and duodenal).

In the four remaining cases definite erosions and pet-echial bleeding points were noted in the stomach and duodenum. The age of the patients ranged from 1 to 33 years, the majority being about 5. The time of death after fracture varied from one to eighty three days, both occurring within three weeks from the time of fracture in all but five cases. Hemorrhage from the gastrointestinal tract recognized clinically and recorded as hematemesis or melena, was observed in twelve of the twenty nine cases tabulated in five additional instances autopsy revealed evidence of bleeding not recognized clinically. Usher therapy was instituted in seven cases diagnosed clinically two of these patients recovered completely. One patient (I W Hospital No. 6974) a 36-year-old man, having sustained multiple fresh fractures in an automobile accident, was admitted to the University Hospital on Dec. 10, 1940. It was demonstrated in

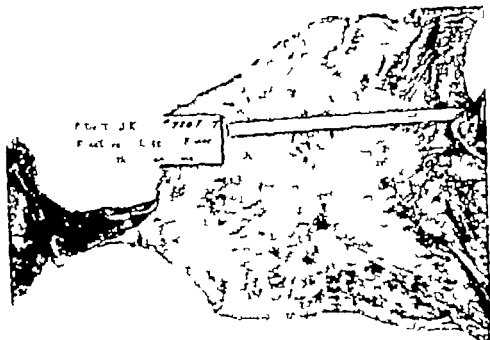


Fig. 1.—Stomach with simple gastric ulcers (see Table 1, C) from fracture of the left rib. Basal diagnosis was peritonitis. The hemorrhage on the right hand 1 day and the patient died on

the urine of the patient the last full wing admission but no abnormal lipemia was observed. He suffered one episode of dizziness. On the twenty-second hospital day hematemesis occurred of the following melena, which continued for one week, necessitating blood transfusions. The prothrombin time and vitamin C level in the blood were normal. The patient eventually made a satisfactory recovery and was dismissed to his home. There had been no antecedent history of ulcer or bleeding. Another patient (I N Hospital N 7188, 8) a 62-year-old man, was admitted to the General Hospital on March 27, 1949. Melena occurred thirty days before a fresh fracture of the neck of the right





Y	R.D.	Age	Sex	Left fem neck	0	66	Minimal duodenal ulcers, small intestine killed in blood	Small intestine	thick periton
10	A.H.	60	M	Rt (bwa and fibula, compound and comminuted)	0	4	Gastric ulcer cm	Vaginal tumor 10 days on "red day"; died gas bacillus infection	
11	A.O.	42	M	2nd Lumbar vert ltra	0		duodenal ulcers, 1 cm	Lat use (col) 1 time f fracture	
12	M.McD	64	M	Left femur inter trecha (tibia), comminuted	+	3	Mild pleuropneumoniae gas in erosions, 5 mm	Hematemesis 3rd day died f bronchopneumonia	
13	O.A.	60	M	L.R. nt 4 10 D	+	16	Perforating 1 ulceral ulcer 25-30 mm no perforation blood intestinal tract	Admitted to hospital 11th day with acute abscess mediastinum, typhoid	
14	E.B.	63	M	Rt fem head, fracture 1 block from	0	11	Several prepyloric ulcers, 4-6 P valvula ileus		
15	R.L.	78	M	Rt humerus	0	19	Posterior duodenal ulcer 1.5 cm no perforation	Died coronary occlusion	
16	K.R.	62	F	Left femur sub trecha (tibia)	+	14	Perforating ant posterior duodenal ulcer 1.5-2 cm soft area subsequent d perforation f ulcer f gas abscess, gastritis	10th day with subsequent d perforation f ulcer f gas abscess, gastritis	
17	M.L.	17	M	Rt femur, compound	+	-	Gastric ulcer rhagades erosions anal wall plus bleed by post	Hematemesis 10th day at fatal time from h. a. et f.	
18	B.L.	91	M	Left femur supra penular	0	10	Duodenal ulcer rounded edges	Died f pneumonia	
19	O.J.	0	F	Rt. femur compound	0	73	Duodenal ulcer 0.5 cm no perforation	Fixation f f m with Rault's Peterson nail	

TABLE I. SUMMARY OF CLASH PARAMETERS ABOVE GAMMA-ENERGICAL ULTRA-ANISOTROPY EXPERIMENT IN PATENT W 0 DIED EARLY AFTER  
PARAMETERS OF LOW-BURST, TENSILE WITH TWO CLASH WITH BURNOUT

	TIME	AGE (YR.)	SEX	RACIOMETER REFS	CLINICAL EVIDENCE OF AT LEAST ONE ILLNESS (+ OR 0)	ELK INTERVAL BETWEEN FRANCHISES (DAYS)	SYMPTOMATOLOGICAL FINDINGS	AF	KS
1	15 W	66	P	Left femur		44	Multiple areas gastric ulcers 1 cm no indication		Intermittent the follow 10 day after manipulation and cast f fracture
2	B H	53	I	Rt tibia	0	14	Posterior diaphyseal ulcer—4 mm., punched out no adhesion from		Manipulation and cast f fracture
3	J McD	75	M	Bilateral tibia and fibula, and pelvis	0		Posterior diaphyseal ulcer 1 cm		Marked cerebral fct embolism f anisotropy
4	U C	4	M	Ribs and pelvis	0	14	Anterior diaphyseal ulcer 8 mm cast		Acute leishmaniasis
5	J W	56	F	Bilateral tibia, fibula, rt radius, left humerus and pelvis	0	1	Anterior processes		Intermittent cases f death unknown
6	O S	60	M	Rt femur cast mangled	0	84	Subcutaneous prepapular ulcer 5 cm, hemorrhagic base slightly raised edges		Died 3 da after mass resection f fracture cerebral fat embolism at autopsy
7	J P	64	M	Left lb and rt tibia	0	7	Prepubertal lesion, 5 mm 5 diaphyseal ulcers, 3 cm indication, hemorrhagic		Myelitis history
8	J M	67	M	Rt tibia and fibula, and pelvis	+	6	5 hemorrhagic gastric ulcers 5.7 mm with fct bleeding postula, active (1 tract contained old blood		Intermittent 2nd and 6th day with thrombocytopenia and death





THE EXPERIMENTAL PRODUCTION OF GASTRODUODENAL ULCERATION AND/OR  
EROSION IN LABORATORY ANIMALS BY FRACTURE OR CURETTEMENT OF BONE MARROW  
(WITH REFERENCE TO THE ULCER DYSPEPSIA)

The observations made in the clinical cases reported in the foregoing suggested the necessity of determining whether ulcer could be produced in experimental animals by fracture of the long bones. The occurrence of spontaneous gastroduodenal ulceration in dogs is unknown. Accordingly ninety-one dogs were subjected to a drill hole through both cortices of the humerus, with and without curettement of the bone marrow or fracture. Normal adult dogs were employed and the operative procedure was carried out under intravenous sodium pentobarbital anesthesia with sterile technique. The drill hole was made with a power-driven (electric) drill measuring  $1/4$  inch. The diet of the experimental dogs was varied in different series. All dogs were sacrificed with an overdose of sodium pentobarbital twenty-one days after the operative procedure and the gastrointestinal tract was examined in each instance. Forty-five of the ninety-one dogs (49 per cent) subjected to operative fracture of the humerus demonstrated positive gastroduodenal pathology when sacrificed. Ten showed ulcer and/or erosion of the stomach or duodenum (11 per cent). In one instance a perforated duodenal ulcer was observed. The remainder of the forty-five dogs presented a mild to severe gastritis and/or duodenitis, with frequent evidence of hemorrhage from petechial bleeding points. The animals were free of any associated illness and all were sacrificed. The varied diets were found to be of no significance in the incidence of gastrointestinal pathology in the different series of dogs.



Fig. 1. Dog No. 12. The specimen shown is from the stomach and duodenum of a dog subjected to fracture of the humerus. There is a perforated duodenal ulcer. The specimen shows the ulceration of the bone marrow of the humerus.

A series of six guinea pigs weighing 250 to 411 grams, was subjected to fracture of the humerus. All fractures were produced by direct trauma under ether anesthesia. Two of the animals received repeated fractures of other long bones. No restriction of food or water intake was made and the animals were sacrificed from ten to fifteen days following fracture. At the time the gastrointestinal tract was initially examined, one of the six guinea pigs had a gastric ulcer. At equal number of times treated in a similar fashion, no gastro-intestinal pathology was observed.

femur. Associated with the onset of melena, a sudden and marked drop in hemoglobin occurred for which blood transfusions were given. The stool were consistently positive for blood for two weeks. Gastric aspiration without histamine stimulation revealed 18 degrees free acidity and 34 degrees total acidity. The patient had undergone gastrojejunostomy elsewhere eighteen years previously for duodenal ulcer. He had experienced only mild infrequent epigastric distress in the intervening years, but this was the first hemorrhage since operation. X-ray examination of the gastro-intestinal tract with a barium meal sixty days after the fracture revealed a large stomal ulcer 9 cm in diameter. The patient did well on an ulcer regimen and was discharged from the hospital on crutches. X-ray examination three months later demonstrated healing of the stomal ulcer, no crater being made out. There has been no recurrence of ulcer symptoms since the fracture. It was felt that this episode represented an acute ulceration following fracture.

In reviewing the records of the University Hospital from 1920 to 1946 seventeen patients who died early after surgical amputation of the thigh were submitted to necropsy. One patient (D W. Hospital No 737507 Table I) a 55-year-old man, underwent a low thigh amputation with ice anesthesia for arteriosclerotic gangrene of the right foot on Nov. 18, 1943. He died suddenly the following day. Post mortem examination revealed an acute gastric ulcer 1 cm in diameter on the lesser curvature. There was no history of contributory gastrointestinal symptoms. Studies for fat embolism were not done. Another patient (J B) a 60-year-old woman whose records were obtained from the department of pathology files, died seventy-three days after a right supracondylar amputation for arteriovelar rotic gangrene of the right foot. Post mortem examination revealed multiple gastric ulcer 3 to 10 mm in diameter with slightly elevated margins. Similarly there was no history of gastrointestinal disease. In addition, it must be noted that no patient (Case 10 Table I) underwent amputation for compound fracture of the right tibia and fibula.

In response to an inquiry addressed to fifty American orthopedic surgeons concerning the occurrence of post neon hematemesis as a sequel to fractures of long bones, or after manipulative procedures upon bones or joints, forty-two replies were received. One surgeon stated that he had observed a patient in whom sudden hematemesis and melena occurred four days after fracture of the left femur. The patient had undergone surgical closure of a perforated duodenal ulcer sixteen years previously and had no gastrointestinal complaint in the intervening years. The patient recovered under an ulcer regimen and blood transfusions, and had no further difficulty. Another surgeon disclosed having seen a patient in whom a severe and spontaneous gastric hemorrhage followed a laminectomy for protruded intervertebral disc. The patient later underwent a subtotal gastric resection for ulcer. Another surgeon noted three cases of fracture in which a subsequent loss of blood was found to have as its source the gastrointestinal tract inasmuch as blood was found in the stools of these patients. Two surgeons each reported having observed hematemesis once after the manipulation of a stiff joint or contracture under anesthesia. No others reported observing ulcer or hematemesis in patient not previously having ulcer.

muscular administration of histamine in beeswax (15 mg base). Some also received curettage of the bone marrow at the time of operative fracture. No dietary restrictions were imposed and all animals were sacrificed from six to thirty-one days after fracture. Section of the stomach, duodenum, brain, lung and kidney were obtained for microscopic study.

As is noted in Table II, fourteen of the eighteen dogs subjected to a drill hole of the humerus, with curettage of the bone marrow accompanied by histamine-in-beeswax administration demonstrated abnormal gastroduodenal findings in six days or less. Of the fourteen dogs, nine showed definitive gastric or duodenal ulcers (one perforated and one perforating) and two showed erosions of the mucous membrane. Definite bleeding points and hemorrhagic petechiae were noted in the stomach and duodenum of nine dogs. The one dog which sustained spontaneous fracture of both forelegs and was given six daily injections of histamine in beeswax presented a large gastric ulcer when sacrificed in six days. Five control dogs subjected to anesthesia but to no operative procedure presented no pathologic gastrointestinal findings when sacrificed after five and six daily injections of histamine-in-beeswax mixture.

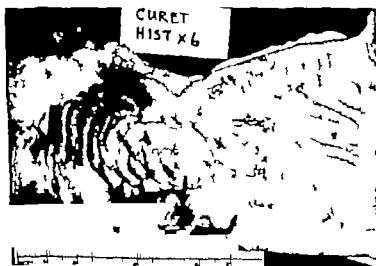


Fig. 1.—Duodenal ulcer and trail bleeding points from Dog 61 (see Table II) subjected to curettage of the bone marrow of the right humerus in addition to daily intramuscular injection of histamine-in-beeswax.

One of the thirteen rabbits subjected to fracture of the humerus accompanied by histamine-in-beeswax administration showed a gastric ulcer when sacrificed in six days.

Microscopic study of the tissues obtained from these animals will be discussed later in this presentation.

#### TIMING OF THE EFFECT OF HISTAMINE IN CLINICAL CASES OF FRESH FRACTURE OF LONG BONES AND AFTER OPERATIVE FRACTURE IN EXPERIMENTAL ANIMALS

1. Study of Gastric Reaction in Clinical Cases of Fresh Fracture.—A review of the data cited in Table I concerning the occurrence of gastroduodenal



Having demonstrated that ulcer and/or erosion of the stomach and duodenum in animals may follow the experimental production of fracture or curettage of the bone marrow, it remained to be shown whether experimental fractures in animals would abet the ulcer diathesis. Ulcers of the stomach and duodenum have been produced in dogs quite consistently in this laboratory over an eight year period employing daily intramuscular injections of histamine-in-beeswax mixture, thus eliciting a maximal gastric secretory response over a period of twenty-four hours after each injection. It was shown by Hay and associates<sup>1</sup> that a forty-day ulcer may be produced regularly in dogs by this method. The average appearance time of the ulcers was twenty-three days. In another series of fourteen control dogs to which 30 mg. of histamine-in-beeswax were administered daily killed from four to fourteen days after commencement of the administration of histamine ulcer was observed in one dog after seven days of histamine. Over an eight year interval during which time histamine-in-beeswax was given to a large number of dogs, ulcer was observed twice at four days following the daily administration of 30 mg. of histamine implanted in beeswax. It was also shown<sup>2</sup> that bona fide ulcers in rabbits cannot be produced with histamine alone. Any condition, therefore, which may increase the susceptibility of the gastric-duodenal mucosa to the erosive action of gastric juice or any circumstance which hastens the development of the histamine-induced ulcer measured by a reduction in time of development to within six days after commencement of daily injections, is considered an abetting influence of the ulcer diathesis. Similarly any condition which favors the development of a gastric or duodenal ulcer in rabbits when histamine-in-beeswax administration is employed may be considered to abet the ulcer diathesis.

Accordingly a study was carried out utilizing twenty-three dogs and thirteen rabbits. Eighteen of the twenty-three dogs were subjected to a drill hole through both cortices of the right humerus with curettage of the bone marrow with a pliable wire under sodium pentobarbital anesthesia (15 mg. per pound body weight intravenously). The operative procedures were carried out under sterile precautions. Administration of daily intramuscular injections of histamine-in-beeswax mixture (30 mg. base) prepared after the method of Code and Vareo<sup>3</sup> was begun the day of operation. Five dogs, serving as controls, were anesthetized but were not subjected to an operative procedure, and received daily injections of histamine-in-beeswax. All animals were fed each morning a standard diet of tablet scraps and dog kibbles, the food pans being removed each evening. Three dogs died four and five days following operation. The remaining dogs were sacrificed in six days or less, and sections of the stomach, duodenum, brain, lung, and kidney were obtained for microscopic study. One additional dog sustained spontaneous fractures of both forelegs when it jumped from its cage on an upper tier of cages to the floor a distance of about seven feet. This dog was then given six daily injections of histamine-in-beeswax and sacrificed at the end of that time.

Thirteen rabbits were subjected to a fracture of the humerus under a venous sodium pentothal anesthesia and received in addition, daily intra-

ulcer in patients with fixation of the long bones suggested the possibility of stimulation of gastric secretion due to histamine liberation from the site of trauma. Studies of gastric secretion were carried out on ten consecutive patients admitted to the University Hospitals with fresh fractures of bone. Gastric secretions were obtained for analyses by gastric intubation of these patients



Fig. 4.—Gastric ulcer and multiple petechial ulcers from Dog 617 (see Table II) subjected to curettage of the bone marrow of the right humerus in addition to six daily intramuscular injections of histamine-hydrochloride.



Fig. 5.—Ulcer and dark ulcer and nasal bleeding points from Dog 603 (see Table II) subjected to curettage of the bone marrow of the right humerus in addition to six daily intramuscular injections of histamine-hydrochloride.

in a fasting state a week after admission to the hospital a possible. Each analysis of gastric acidity (free and total) and volume was made on a one hour specimen obtained by continuous aspiration and repeated on consecutive days. No drugs were administered during the period of aspiration.

Results of these studies are shown in Table III. There is no significant increase in the acidity or volume of fasting gastric secretion following fracture

TABLE II. OCCURRENCE OF GASTROINTESTINAL ULCERS AND/OR EMBOLI IN DOGS SUBJECTED TO DRILL HORN OF THE RIGHT HUMERUS WITH CURTAGE OF THE BONE MARROW ACCOMPANIED BY DAILY ADMINISTRATION OF HIND MILK IN BLENDED MIXTURE

DOG NO	WT (KG)	OPER. TRA. NO. EMBOLUS	ULY DISE. RIB. AMING (MO.)	OP. DRY	RESULTS	REMARKS
545	48	D II <sup>a</sup>	20	4	Duodenal ulcer, one perforated; gastric bleeding points	Died 4th day pneumonia
546	77	D II.	20	3	Duodenal erosion gastric bleeding points	Died 8th day pneumonia
547	90	D II	20	4	Essentially negative stomach and duodenum	Sacrificed 4th day
548	20	D II	20	4	Essentially negative stomach and duodenum	Sacrificed 4th day
549	22	D II	20	6	Perforated duodenal ulcer; gastric bleeding points	Sacrificed 6th day
550	21	D II	20	4	Essentially negative stomach and duodenum	Sacrificed 4th day
551	25	I II	20	3	Duodenal ulcer lesser rhagus gast. n.	Died 5th day emphysema
552	44	I II	20	3	Early duodenal ulcer; utral bleeding point	Sacrificed 6th day
553	1	D II	20	6	Negative stomach and duodenum	Sacrificed 6th day
554	24	I II	20	6	Duodent; utral bleeding points	Sacrificed 5th day
555	19	I II	20	6	Duodenal ulcer	Sacrificed 6th day
556	25	I II	20	1	Hemorrhagic duodenitis	Sacrificed 24 hours
557	20	I II	20	6	Bleeding utral erosion	Sacrificed 6th day
558	26	D II	20	3	Utral bleeding points	Sacrificed 6th day
559	37	D II	20	6	Petechial gastric ulcer and bleeding points	Sacrificed 6th day
560	25	I II	20	6	Early duodenal ulcer	Sacrificed 6th day
561	24	I II	20	6	Mult. ple. gastric ulcers	Sacrificed 6th day
562	14	I II	20	6	Duodenal ulcer and gastric bleeding points	Sacrificed 6th day
563	4	Y operation upon ischium re. rib. fracture f. both fore-legs	20	6	Large gastric ulcer	Sacrificed 6th day
Control (curtaged, hindbone but no curtage of bone marrow)						
1	22	0	20	3	Y ulcer erosion, or bleeding points	Sacrificed 1 1/2th day
2	20	0	20	3	Y ulcer erosion, or bleeding points	Sacrificed 6th day
3	24	0	20	3	Y ulcer erosion, or bleeding points	Sacrificed 6th day
4	19	0	20	6	N ulcer erosion, or bleeding points	Sacrificed 6th day
5	28	0	20	6	Y ulcer erosion, or bleeding points	Sacrificed 6th day

Y = Y-shaped, 1 1/2th curriage of bone marrow.

TABLE III. STUDY OF THE GASTRO SECRETORY RESPONSES IN CASES OF FRESH FRACTURE OF BONES IN MAN (NO HISTAMINE STIMULATION USED)

NO	P. FIFTY	SEX	AGE (YR.)	FRACTURE	NO. OF ANALYSES	RANGE OF FREE ACIDITY*	RANGE OF TOTAL ACIDITY*	RANGE OF VOLUME C.C.
1	M. H.	M	69	Pelvis, acetabulum, or calcus	6	0.0	12.65	3-18
	E. O.	F	7*	Left humerus	4	0.34	14.68	29-107
	C. B.	F	73	Right femur	6	0.4	10.90	8-53
4	A. A.	M	60	Right tal tibia and fibula with manipulation	3	8-10	4-52	103-204
5	A. K.	M	67	Left 10th & 11th ribs and 12th thoracic & 1st lumbar vertebrae	3	0.0	1.56	97-43
6	C. T.	M	63	Rt femur with hip spilling	6	1.3	4.126	10-128
7	H. D.	M	40	Rt knee	5	0.04	14-44	1-133
8	C. McD.	F	65	Left femur (week)	3	0.0	8.130	3-45
9	M. L.	M	17	Right femur	1	0	93	
10	M. G.	F	61	Left femur	6	0.36	18.56	4-31

\* Study of Histamine Secretion Following Operative Fracture of Bones in Experimental Dogs Having Gastric Pouches.—To further ascertain whether fracture of bones may produce an increase in gastric secretion, experiments were outlined employing dogs possessing isolated gastric pouches, on the thesis that a histamine-like stimulation effect would be reflected in the pouch secretions in dogs. Five Heidenhain (denervated) and two Laval (innervated) pouch dogs were used. Under intra-venous sodium pentobarbital anesthesia six pouch dogs (five Heidenhain and one Laval) were subjected to drill holes with curettage of the bone marrow of the right humerus under sterile technique, the animal having been fasted eighteen hours prior to the experiment. All conditions were similar to those carried out in the preceding operations with dogs. Gastric pouch secretions were collected for a one and two-hour fasting period, following which the animal was anesthetized and the operative procedure performed. Hourly samples of pouch secretions were collected during the operation and for four subsequent hours. Studies of pouch secretions were made on these dogs every other day for four hours for ten days. For control experiments one Heidenhain and one Laval pouch dog were subjected to nonspecific operations (appendectomy and splenectomy, respectively) and pouch secretion studied in the same manner as in the experimental dogs. On the day of operation on all dogs in this trial control blood histamine values were determined as well as during and following the operation and in some cases of subsequent laboratory blood values were maintained throughout the course of the experiment.

The results of this group of experiment are recorded in Table IV. It is noted that in only one dog (No. 14 H) was there a marked stimulation of

of bones. Thus, there does not appear to be a stimulation of gastric secretion due to liberation of histamine at the fracture site as measured by gastric analyses. Ranges of gastric acidity and volume in the data recorded are in

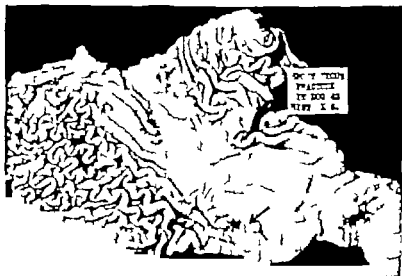


Fig. 6.—Gastric ulcer on Dog 43, 11th accidental fracture of both wrists subjected to six days intramedullary injection of histamine-in-bones. Arrow shows large atrial ulcer.

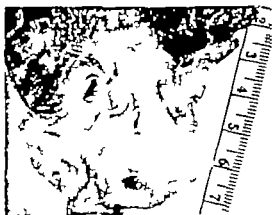


Fig. 7.—Gastric ulcer from Rabbit subjected to four to five fractures and swellings of the bones marrow of the ribs accompanied by six to seven intramedullary injections of histamine-in-bones six

accord with normal values occurring in patients of similar age groups. It is to be noted that one patient (No. 9) in Table III is the same patient as one (No. 17) in Table I. Due to the occurrence of gastric hemorrhage after admission to the hospital, only one analysis of gastric acidity was determined.

analyses of free acidity of the three control dogs were not significant. Unlike the experimental dogs. Examination of the stomach and duodenum in the experimental dogs revealed the occurrence of erosion and/or ulcer or evidence of ulcer by healing scars in five of the fifteen dogs. The three control dogs displayed no abnormal findings upon sacrifice. It was noted also that the acute or active gastroduodenal lesions were present when the animal was sacrificed in three and four days, while lesions displaying chronicity occurred in ten, twenty and twenty two days, respectively. Mild gastritis and duodenitis were somewhat common findings. Microscopic findings are described later.

TABLE IV THE EFFECT OF EXPERIMENTAL FRACTURE UPON THE GASTRIC SECRETION RESPONSE IN INT CT DOGS

DATE	DOG NO	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144
5/17		0 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>	13 <sup>+</sup>	0 <sup>+</sup>	41 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>	20 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>	41 <sup>+</sup>	50 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>	0 <sup>+</sup>
5/18		0	0	0	0	0	20	0	0	0	0	0	0	31	0	36	0	0	0
5/19		0	0	0	0	0	0	0	0	31.3	0	0	0	0	0	0	0	43	0
5/20		0	33	0	0	0	60	20	18	0	0	0	0	32	3	0	0	56	0
5/21		0	0	0	0	4	0	0	7.8	0	0	0	0	16	0	0	0	38	0
5/22		0	0	0	0	6	4	4	10	0	0	0	0	0	0	0	35	0	23
Operation																			
5/23		0	0	0	0	0	0	0	0	0	0	9	0	5	7.5	4	0	10	10
5/24		1	0	0	0	0	0	0	0	0	0	0	0	86	0	0	0	0	0
5/25			0	0	0	0	0	0	0	0	0	0	0	0	0	73	0	0	0
5/26				0	21	0	0	0	7.5	0	0	0	0	0	0	0	0	0	0
5/27					6	0	48	0	10	0	0	0	0	0	51	0	0	0	75
5/28					3	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5/29						0	0	0	0	0	0	0	0	0	0	0	0	0	0
5/30							0	0	1	0	0	0	0	0	0	0	0	51.3	0
6/1								0	0	0	0	0	0	0	0	0	0	0	0
6/2									0	0	0	0	0	0	0	40	0	0	0
6/3										49	14	0	0	0	46	0	46	0	64
6/4											4	0	0	0	3	33	15.3		
6/5												0	0	0	30	0	60	0	
6/11													4	4	0	73	0	1.3	
6/12														0	0	0	0	0	
6/13															0	15	0		
6/17																0	0		
6/18																0	0		

ity of gastric juice obtained  
drill hole over that of the bar-  
reloramus operation. Term of  
operation procedure was carried  
the 24 hours after operation.

It was concluded from these experiments that histamine liberation from the fracture site is not sufficient to cause stimulation of gastric acidity necessary to produce the gastric and duodenal lesions found in patients with fresh fracture or in the experimental dogs subjected to partial fracture.

#### DUODENAL PRODUCTION BY THE INTRAVENOUS INJECTION OF FAT INTO EXPERIMENTAL ANIMALS

On the basis that the acute gastric and duodenal ulcers occurring in patients and animals sustaining or receiving fractures of long bones may be associated with the occurrence of embolism of fat, a study was utilized to determine whether ulcer could be produced experimentally by the intravenous injection of fat.

TABLE IV THE EFFECT OF VARIOUS OPERATIONS ON POUCH SECRETIONS IN DOGS

DOG NO	OPERATION	EFFECT
<i>None Operations</i>		
145 (H)	Drill hole operation, rt humerus	Marked stimulation of acid and volume for 6 days post operatively
120 (H)	Drill hole operation, rt humerus	✓ stimulation effect
15 (H)	Drill hole operation, rt humerus with destruction of the marrow by means of pliable wire	N stimulation effect
50 (H)	Drill hole operation, rt humerus with destruction of the marrow by means of pliable wire	N stimulation effect
132 (H)	Operative fracture rt humerus	✓ stimulation effect
116 (P)	Operative fracture, rt humerus	N stimulation effect
<i>Non-specific Operations</i>		
20 (H)	Appendectomy	N stimulation effect
10 (P)	Splenectomy	N stimulation effect
*This effect of marked stimulation not present here operation as reported in four weeks		

gastric acidity and volume 1 to 4 postoperative days. This was repeated in the same dog at a later time at which time no stimulating effect was noted. The blood histamine values showed no significant variation from normal levels.

**3 Studies of Gastric Secretions in 1 to 4 Dogs Subjected to Operative Fracture With 1 Series of Gastrointestinal Findings and the Occurrence of Fat Embolism**—The following experiment was performed on a group of eighteen intact dogs having been placed on a standard diet of  $\frac{1}{2}$  pound horsemeat, 1 pound dog kibbles, per day and water as desired. Experiments consisted of daily gastric intubations and aspiration of gastric juice for determinations of free HCl, total acidity and reaction in terms of pH. After a period of standardization of six days, fifteen of the eighteen dogs were subjected to drill holes of the right humerus under intra-earous sodium pentobarbital anesthesia employing the technique. The control dogs were anesthetized only; no operative procedure was carried out. Daily gastric aspirations were carried out in all dogs until the completion of the experiment. The animal was sacrificed by an overdose of barbital at regular intervals over a period of four weeks following the operative procedure. The three control dogs were sacrificed at six, twelve and twenty-eight days of operation, respectively. All dogs were fed the standard diet each morning after gastric aspirations and food pans were removed each evening. Following operation no food was allowed until after the gastric aspiration of the following day. Water was allowed all dogs at all times. Upon sacrifice of each animal the gastrointestinal tract was examined and sections of the stomach, duodenum, brain, and lungs were obtained for microscopic study with reference to the occurrence of fat embolism.

Results of this study are recorded in part in Table V. It is noted that the determinations of free acidity before and after the drill hole operation of the humerus displayed no demonstrable differences in degree. Similar gastric

ulcerous injection of fat all developed multiple bleeding duodenal and gastric ulcers within three days after the first injection of histamine.

In addition four dogs, each possessing a gastric pouch, received a single intravenous injection of fat. Studies of gastric secretion in a fasting state before and after injection of fat were carried out in each dog. It was found that intravenous injected fat does not stimulate nor augment gastric secretion.

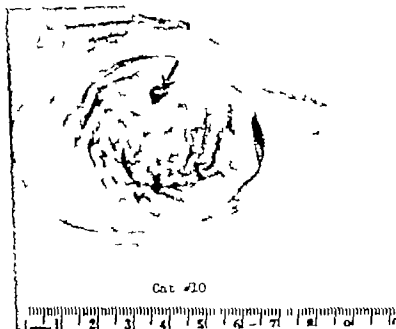


Fig. 1. —Gastric ulcer from Cat #10 subjected to single intravenous injection of nonemulsified human fecal fat (1.5 per kilogram) sacrificed in four days.

# 1. THE ROLE OF FAT EMBOLISM 2. THE OCCURRENCE OF GASTRODUODENAL ULCER AND OR PERFORATION FOLLOWING FRACTURE IN PATIENTS AND EXPERIMENTAL ANIMALS, WITH REFERENCE TO THE RATE OF INTRAVENOUSLY INJECTED FAT

To determine the validity of the theory that fat emboli are released from the site of fracture and lodge in the vessels of the gastrointestinal tract thus producing a local area of mucosal anemia susceptible to the acid peptic digestive action of gastric secretions, sections of tissues involved were examined microscopically. Single blocks of tissue from the stomach, duodenum, brain, lungs, and kidneys were taken from several groups of animals in the previous experiments, as well as from a number of patients who died early after fresh fracture of long bones. Tissues were fixed in Zenker's solution, frozen and stained with Eosin III. Emboli of fat thus are demonstrable as orange-colored globules within the blood vessels.

1. The occurrence of fat embol attending the intravenous injection of fat in fifty-two animals is represented in Table VI. The influence of the time inter-



Observations were carried out in twenty-nine animals consisting of eleven rabbits, six cats, two guinea pigs, and ten dogs. Human boar or oriental fat was employed, obtained from surgical procedures, and extracted with ether. Fat,  $1\frac{1}{2}$  cc per kilogram of body weight was injected intraneously. It has previously been stated that rabbits are quite resistant to ulcer production by histamine alone. In each of six rabbits, whose weights averaged 1.74 kilograms, a single intravenous injection of 15 to 20 cc of fat was made. Then 30 mg of histamine-hydrochloride was implanted once daily for from one to four days.

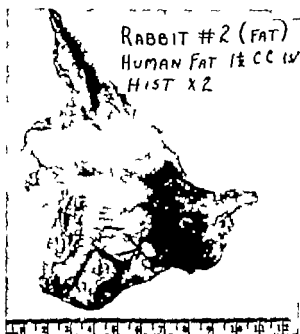


Fig. 2.—Perforated ulcer in stomach of rabbit after single injection of 15 cc of human (oriental) fat intraneously, in addition to two daily intravenous injections of histamine-hydrochloride.

No dietary strictures were imposed on the rabbit. A perforating ulcer occurred in each instance and one of that rabbit died of pulmonary embolism shortly after the fat injection. Three rabbits were injected with fat but were given no histamine. Ulcer did not develop. In two additional rabbits, a daily implantation of 30 mg of histamine-hydrochloride was made, in one over a period of twenty-one days, in the other for twenty-eight days; neither developed ulcer. Of six cats, each receiving a single intravenous injection of fat, two developed gastric ulcers, one at four the other eighteen days after the fat injection. Of two guinea pigs injected with fat, both exhibited typical gastric ulcers. Of seven dogs given a single intravenous injection of fat, a bleeding duodenal ulcer was found in one dog sacrificed fifteen days after the fat injection. Of three dogs that received 30 mg of histamine-hydrochloride daily following single

lung and the antrum and corpus of the stomach of these animals were examined. Three of these dogs had been controls, no operative procedure being carried out. Sacrifice of these animals ranged from one to twenty-eight days following the drill hole through the humerus. Fat emboli were demonstrable in the lung only in those dogs sacrificed six days or less after the operative procedure and, in one instance, fat embolism was noted in the vessels of a stomach in which there were numerous punctate hemorrhagic areas in the mucosa.

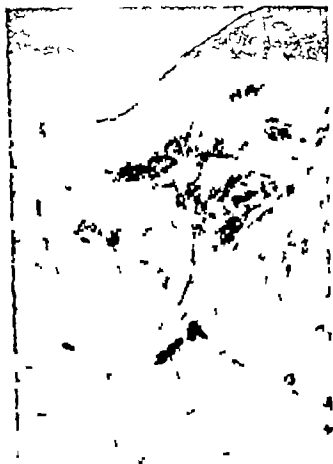


Fig. 1. — Photomicrograph illustrating embolic fat in subcutaneous tissue under the skin of a dog from the stomach of a dog subjected to extraction of the bone marrow of the right humerus and few daily intravenous injections of a standard emulsion (Sudan III stain, magnification 100 X).

Studies relative to the incidence of fat embolism in patients were made on tissues of the stomach, brain, lungs, and kidneys, stained with Sudan III obtained from the autopsy material of twenty-three patients, nineteen of whom died early after fresh fracture of the long bones. The incidence of the occurrence of fat embolism in the various tissues of these patients is shown in Table

TABLE VI. INFLUENCE OF TIME INTERVAL OF OCCURRENCE OF F &amp; EMBOLI ATTENDING THE INTRAVENOUS INJECTION OF F &amp; E IN LABORATORY ANIMALS (DOGS, CATS, RABBITS, VS GUINEA PIGS)

No. of Animals	AMT OF INJECTED ( PER KG )	PER CENT OF TISSUES REVEALING F & E EMBOLI				
		LUNGS	BRAIN	KIDNEY	STOMACH	
Sacrificed 1 to 4 d vs after fat injection						
A.	23	1½	91	60	73.0	47.8
Sacrificed 5 to 21 days after fat injection						
B.	29	1½	41	11.1	24.4	37

val, between the fat injection and the sacrifice of the animal, upon the incidence of demonstrable fat embolism in the various tissues is also shown. It is to be noted that the identification of fat in the stained sections was considerably higher especially in the stomach, in the animals sacrificed and studied within one to four days after the fat was injected intravenously. In several instances, fat emboli within the submucosal vessels of the stomach were seen near or underneath the ulcers.

TABLE VII. OCCURRENCE OF F &amp; EMBOLI IN THE TISSUES OF DOGS SUBJECTED TO DRILL HOLE WITH CURETTAGE OF THE BONE MARROW OF THE HUMERUS, ACCOMPANIED BY HISTAMINE IN BONEWAX ADMINISTRATION

NO. OF DOGS	PER CENT OF TISSUES REVEALING EMBOLI			
	LUNGS	BRAIN	KIDNEY	STOMACH AND DUODENUM
Sacrificed 2 to 6 days after operative procedure				
19	63.4	26.3	47.4	24.3

Microscopic studies were carried out in nineteen animals (presented in Section B) which were subjected to drill hole and curettage of the bone marrow of the humerus accompanied by histamine administration. Single blocks of tissue from the stomach, duodenum, brain, lungs, and kidneys were examined. These animals were sacrificed from two to six days after operative fracture. The incidence of demonstrable fat embolism in the various tissues of these animals is shown in Table VII. In one instance fat globules were seen in the submucosal vessels immediately below an ulcer. In another instance, small fat particles were noted in mucosal capillaries under a superficial erosion of the stomach.

Microscopic studies were carried out on another group of experimental animals, eighteen dogs in which studies of gastric secretion following peritoneal fracture had been carried out (Section C 3). Single blocks of tissue from the

TABLE VIII. INCIDENCE OF THE OCCURRENCE OF F &amp; EMBOLISM IN PERITONEAL FRACTURE OF LONG BONES

NO. OF ANIMALS	PER CENT OF TISSUES REVEALING F & E EMBOLI			
	LUNGS	BRAIN	KIDNEY	STOMACH
19	44.5	4.3	15.7	40

A seven day interval between fracture and death, 7 days.

\*Single blocks of the stomach were examined microscopically in three cases; six showed definite evidence of fat embolism in the mucosal and submucosal capillaries.

autopsy at which time the diagnosis was substantiated. The incidence of hemorrhage from the gastrointestinal tract in the cases presented was 59.6 per cent being recognized clinically in 41.4 per cent.

It should be mentioned that a great number of fracture patients submitted to necropsy died almost immediately following the injury—too short a time for the occurrence of gastroduodenal ulceration from fat emboli. Similarly ulcers may be healed over in cases coming to necropsy late after fracture.

It is apparent when an attempt was made to place the observation made initially upon an experimental basis that ulcers can be produced by experimental fracture and drill hole with urettag of the bone marrow in the dog, an animal in which the spontaneous occurrence of ulcer is not known. Moreover when gastric secretion is stimulated maximally by the administration of histamine implanted in beeswax, the rate of occurrence is increased. Conversely subjection of the animal to operative fracture hastens the development of the histamine-beeswax provoked ulcer in the dog. Similarly when rabbits are subjected to fracture in addition to histamine administration, gastroduodenal ulcers may be produced, a result which is not obtainable in rabbits receiving histamine in beeswax alone. Thus it may be said that experimental fracture or urettag of the bone marrow bet the ulcer liability.

One of the thirteen rabbits subjected to fracture accompanied by histamine in beeswax administration developed a gastric ulcer. A higher incidence may have been expected except as Scriba pointed out that the femur of a 2 kilogram rabbit contains an average of only 1.3 gm of fat.

In the studies in which experiments were designed to determine the mechanism of the production of gastroduodenal ulcer and erosion following experimental fractures in animals it is found that stimulation of gastric secretion by histamine liberation from the site of trauma is not a significant factor. Gastric secretory values of free and total acidity and volume as well as blood histamine levels in both intact and injured dogs subjected to operative fracture indicate little if any departure from normal values.

The reproduction of the phenomenon of fat embolism occurring in fracture by the employment of intravenous injection of fat in animals, with and without administration of histamine reveal similar findings as those present in animals subjected to actual fracture—urettag of bone marrow. The intravenous injection of fat does not augment gastric secretion as studied in such dogs.

Finally the demonstration of fat emboli within the submucosal and mucosal vessels of the stomach and duodenum in addition to the organs of the animal receiving experimental fracture as well as in the organs of a number of patients dying early after fracture and amputation leaves little doubt that the occurrence of gastroduodenal ulcer and erosion following fracture of long bones is a concomitant of fat release from the site of fracture. The mechanism of ulcer production following fracture then is undoubtedly that of plugging the end vessel of the mucosa with resultant anemic areas in the mucosa become less resistant to injury and laceration by the acid-peptic juice of the stomach, than is the normal mucosa.

VIII The four control studies, carried out in patients who died of barbiturate poisoning, lobar pneumonia, epilepsy and exposure to cold, exhibited no evidence of fat embolism microscopically.

It is noted that emboli of fat were demonstrable in the vessels of the lung in a greater incidence than observed in other organs studied. Single blocks of tissue from the stomach of fifteen of the patients who died early after fracture revealed an incidence of 40.0 per cent of emboli of fat within the submucosal or mucosal vessels in the stomach. Pyloric mucosal bleeding was seen microscopically adjacent to a mucosal vessel of the stomach occluded by a fat embolus.



FIG. 1. Photomicrograph illustrating emboli of fat in the vessels of the stomach. (See table I, page 157.) The patient, a 35-year-old male, died 10 days after fracture of the right femur. Mucosa hemorrhaged, petechiae of the skin were noted on the third hospital day. At autopsy there was evidence of extralobar fat embolism.

#### DISCUSSION OF THE RESULTS

(Observation of hematemesis from past duodenal ulcer and the onset complicating fracture of long bones prompted this study of case records of patients who died early of fracture (reports collected from the files of the Department of Pathology of the University of Minnesota). The incidence of acute gastroduodenal ulceration in cases of fresh fracture of long bones coming to autopsy over a twenty-five year period was 27 in 1432, or 18.8 per cent. In well over one-half of the cases collected in this study, pathologic diagnosis of fat embolism per se was noted or appeared to follow the course of the illness of each case. Retrospect is highly suggestive—a majority developing dyspnea, mental confusion, oliguria with exfoliating petechiae of the skin, hematemesis, and melena. Clinical diagnosis of acute fat embolism or institution of specific therapy were made in seven (41 per cent) instances, five coming to

embolic occlusion of the vessels to the mucosa by fat released from the fracture site the resultant anemic areas in the mucosa become susceptible to the acid peptic digestive activity of the gastric juice

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It is interesting to note in animal studies at various intervals after the intravenous injection of fat, that the rate of disappearance of the fat from the mucosal and submucosal vessels is rapid. This circumstance undoubtedly accounts for the fact that hematemesis, erosion, or ulcers have not been observed more commonly to accompany fracture of long bones in man.

#### SUMMARY

1. A study of the incidence of gastroduodenal ulcer and/or erosion complicating fracture and amputation of long bones in man was made. A tabulation of twenty-seven cases of acute gastroduodenal ulcer or erosion in patients following fracture of long bones among 1,432 cases of fracture over a period of 76½ years, together with two such cases with recovery is presented. Two similar cases following amputation are also presented.

2. A study was made concerning the experimental production of gastroduodenal ulceration and/or erosion in laboratory animals by fracture or curettage of the bone marrow, with reference to the ulcer diathesis.

3. Studies were carried out concerning gastric secretion in clinical cases of fresh fractures of long bones and after operative fracture in experimental animals, together with studies of the histamine levels of the blood after experimental fractures in animals.

4. Experiments regarding ulcer production by the intravenous injection of fat into experimental animals were carried out, constituting a reproduction of the phenomenon of fat embolism in experimental animals.

5. Microscopic studies were carried out to evaluate the role of fat embolism in the occurrence of gastroduodenal ulcer and/or erosion following fracture in patient and experimental animals, with reference to the fate of intravenously injected fat.

#### CONCLUSIONS

1. Gastroduodenal ulcer and/or erosion, with resultant hemorrhage, are an occasional complication of fracture and amputation of long bones in man.

Gastroduodenal ulcers and/or erosions can be produced in experimental animals by operative fracture or curettage of the bone marrow; the incidence of such erosions or ulcers is markedly increased when histamine administration accompanies the fracture, especially in dogs. Experimental fracture of long bones abets the ulcer diathesis.

2. Gastroduodenal ulcers and/or erosions can be produced by the intravenous injection of small amount of fat; this reproduction of the phenomenon of fat embolism also increases the susceptibility of the laboratory animal to the histamine-provoked ulcer.

3. Emboli of fat can be demonstrated in the submucosal and mucosal vessels of the stomach and duodenum, not only in experimental animals subjected to operative fracture but also in patients dying early after fracture of long bones. The rate of disappearance of the fat from the tissues is rapid.

4. The mechanism of the occurrence of gastroduodenal ulcer and/or erosions following fractures and amputation of long bones is undoubtedly one of

embolic occlusion of the vessels to the mucosa by fat released from the fracture site the resultant anemic areas in the mucosa become susceptible to the acid peptic digestive activity of the gastric juice.

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## Editorial

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### A New Policy

**B**EGINNING with this issue *SUMMARY* will each month contain a signed editorial dealing with some aspect of medicine, surgery, experimental science. Some of these will deal with the work of the author, some will be of the general informative type, while others will without doubt be provocative. In order that the objectives be reached, the editorial policy will be as catholic as possible. There is a dearth of good writing in many of the papers now being published in our journals. There is a shocking lack of propriety by many authors in failing to give proper credit for well-deserved priority. There is all too frequently an unnecessary verbosity in our papers, so that not only are paper and print wasted but the reader's time is unnecessarily wasted. Too frequently conclusions are not based upon the data presented, and all too frequently significance is attached to data that are not significant. The statements made in a paper are often accepted as true merely because one or more of the authors is well known. A preliminary report to gain priority is often not published as a preliminary report, and yet time and again a subsequent report is published because additional studies fail to verify the original statements. The responsibilities of authors to their reading audience are great but not always fulfilled. These are matters of real concern to many of the people interested in the best aspects of medicine in its broadest sense. This editorial is to be published will not be agreed with by all our readers. We hope that they will be would be foolish, nor does *SUMMARY* accept any responsibility for what each author says. We shall engage in no polemics, but we shall be happy to hear from those of our readers who believe that the subjects are not fully presented.

—I. B. RAY

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### ANNOUNCEMENT

In this issue a new department is being established—*Surgical Technique*. The most recent developments in surgical technique will be published. It is the intention of the editors and publishers to give priority to articles of this nature in order to make available to the profession the latest advances in surgery.

# SURGERY

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## Original Communications

### *Society of University Surgeons*

#### THE POSTWAR TRENDS IN THE TRAINING OF THE GENERAL SURGEON

ROBERT M. ZOLLER, M.D., COLUMBUS, OHIO

THE trend toward specialization which started during the World War II has been a most significant one in this country. It is in many ways the diminishing rank of the general practitioner are a direct result of both lay and medical press. Many of these articles point out the inadequacy not only of the practitioner of general medicine but of general surgery. It is especially in the situation of the smaller communities. In these days of intense specialization by anatomic system will there continue to be a need for the so-called general surgeon? The general surgeon notes the increasing anatomic specialization of the various surgical specialties and wonders if the future will limit what he holds altogether. Does the scope of the general surgeon in look as some have defined it the abdomen only? Is limiting the pelvic organs the least fitting work and the soft tissues of the trunk and extremities? Actually there is a trend now to limit his activities principally to the gastrointestinal tract and even this system partially included in the province of proctology which has stalked out of his domain to include the entire colon.

It is apparent that the scope of the function of the general surgeon of the future is a serious consideration. This is a challenging problem of those interested in graduate training and it has a direct bearing on the preparation of the medical school factors making a most significant role in the future of the general surgeon. It is an argument for the future of the general surgeon.

The purpose of these remarks is to present a series of points which will present a picture of the general surgeon of the future. It is hoped that it will point out some of the difficulties involved in setting up the training program for the general surgeon of the future. The postwar trends will be in some of the following directions: (1) the country and the hospital, the type of training which the majority of the surgeons will receive. An attempt will be made to determine how current graduate training fits the needs of the

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The purpose of this communication is to present a series of points which will present a picture of the general surgeon of the future. It is hoped that it will point out some of the difficulties involved in setting up the training program for the general surgeon of the future. The postwar trends will be in some of the following directions: (1) the country and the hospital, the type of training which the majority of the surgeons will receive. An attempt will be made to determine how current graduate training fits the needs of the

practicing general surgeon. We can reach no conclusions which the immediate future might not alter but perhaps a discussion of the situation as it exists today might help to plan more effectively for tomorrow.

The urgencies of war telescoped and disrupted the resident training programs, and since the war the influx of returning veterans desiring further work leading to Board certification has resulted in a confused educational picture throughout the country. It is difficult to determine from the various published data the details of training offered at the present time. In order to procure information which might prove of value to those interested in the development of general surgeons, the following surveys were made:

First, a questionnaire was submitted to the chiefs of over fifty teaching centers in this country asking for details regarding their postwar training program for the general surgeon. They were also asked to state what specialties they thought should be included in such a plan and, finally, to define the scope of the general surgeon today. The response was most instructive and gratifying.

Second, a small number of certified general surgeons practicing in towns of 15,000 to cities of 3,000,000 population from coast to coast were asked to submit the distribution of their work by system over a period of one year July 1, 1946, to July 1, 1947. These men were interested in the problem and spent much effort in analyzing their work for us. This should provide a sound basis for judging those phases of training requiring emphasis.

Finally permission was graciously granted by the Secretary of the American Board of Surgery to review the graduate background of 100 recently certified members of this board. This information can be compared with the plans for postwar training.

According to this survey the majority of the professors of surgery in this country are emphatic in their opinion that the trend toward ultra specialization is undesirable in the training of the general surgeon of the future. They believe a thorough background should be provided in the basic sciences, as well as experience in most of the surgical specialties. They feel that the general surgeon should be competent in dealing with the common problems of thorax, abdomen, and extremities, even though he may eventually limit his field. It would appear possible to discern four training policies:

1. The first program includes a broad experience on the specialty services such as urology, orthopedics, fractures, gynecology, etc. which provides a knowledge of these fields as a background for the practice of general surgery.

The second plan offers more limited training in the specialties and more emphasis upon teaching and research. Attention then is focused upon the special surgical interests of the chief of the service. Such services stress the development of an academic career.

3. The third group of services insist upon an elastic program. They encourage the young surgeon to concentrate upon the aspect of surgery which is of particular interest to him.

4. The fourth group depends largely upon training by preceptorship under one or more certified surgeons.

By each of these training policies, sufficient time is allotted to meet the Board requirements for basic science training. Although men from all groups may eventually become certified as general surgeons, the range of their capabilities are undoubtedly extremely variable. For example an analysis of the qualifications of 100 Diplomates of the American Board of Surgery in 1947 shows a wide diversification of graduate work. The disrupting effect of the war is demonstrated by the fact that 49 of the 100 had credit for service in the armed forces. Of those who received three or more years of training after internship, about one-half received all of their training in the same institution. Fifteen of the entire 100 had five years of hospital training after their internship. Thirty-one received some credit for an assistantship.

The American Board of Surgery is one of the most liberal of the specialty boards. To be sure four years or more of graduate training are required after internship but there are no hard and fast regulations governing the distribution of work done by the candidate during this time. For example a surgeon may be certified with little or no time devoted to urology, fractures, and gynecology or he may devote as much as one year to one particular specialty. On the other hand the Board has demonstrated in its examination questions, that it expects its Diplomates to possess some knowledge of the specialties. The majority of the other specialty boards appear to be more rigid in their recommendations, and some require one or more years of general surgery as a prerequisite to specialty training. This is highly desirable even though it complicates the training program in general surgery and such complications will undoubtedly multiply as an increasing number of young surgeons seek specialty board certification.

Some insight into the postwar trend of training in general surgery can be gained from a study of the outline of the services provided by forty-eight of the leading teaching centers in this country. Fifty-two university clinics and six large private clinics gave detailed information which is utilized in this report. An analysis of these graduate training programs in general surgery is graphically presented in Figure 1.

Eighty-four per cent set a fixed period usually four to six months for pathology or one of the basic sciences, while the remaining 16 per cent depended upon weekly conferences and seminars throughout their training program to provide the background.

With few exceptions, two years or longer was devoted to general surgery. It was impossible to determine the ratio of time spent on clinical ward as compared to the private ward. Prosthetic, pediatric, surgery, plastic surgery, and thoracic surgery were often included in this general surgical service while fractures and orthopedics, urology, gynecology, and neurosurgery were usually separate services. In a few of the universities and in most of the private clinics, six months or more was spent in the outpatient or diagnostic line. However in the majority the outpatient work was integrated with the general service.

Approximately 90 per cent of the training program surveyed provided time in thoracic surgery. Forty-six had a time allotment of three to six months

perceptually set aside for this. It can be seen from the foregoing that basic science, general surgery and thoracic surgery were universal features of the training programs. The other specialties have not fared so well. For example, approximately 77 per cent of the teaching centers indicated that training was given either in otopharyngology or in the management of fractures, or both. Urology was offered in approximately the same number (60 per cent) and neurosurgery by 60 per cent. Experience in podiatric surgery was included in one-half the services, while only 4 per cent provided training in gynecology. Experience in plastic surgery was perceptually included in 40 per cent of the services. Rotation in anesthesiology and roentgenology was offered periodically.

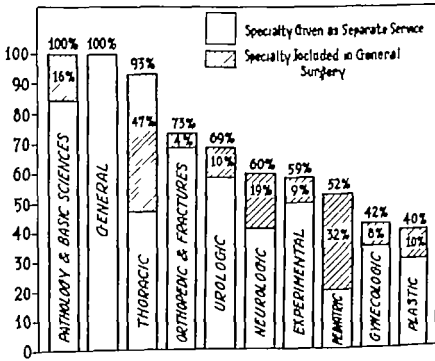


Fig. 1. — Percent of training programs offering various specialties as separate services or included in general surgery.

It should be noted that the training programs, as they now exist, do not consider all of the specialties which the expressed belief of the teachers of surgery and anatomy indicate are necessary for the needs of the practicing general surgeon. Let us consider the specialties which should

The opinion was commonly expressed that the surgeon should open the abdomen first and foremost. The necessity of use of the thoracic approach for lesions of the upper gastrointestinal tract makes it mandatory for the surgeon to be thoroughly familiar with the principles of thoracic surgery. Nearly all of the centers have been able to provide thoracic surgery training.

Treatment of the extremities was invariably regarded as being within the scope of general surgery and it was the opinion of the majority that it is highly desirable for the young general surgeon to receive training in the management of fractures. Matthes (1) pointed out in a panel discussion on emergency surgery presented before the American Medical Association in June 1947 that almost 8 per cent of our population is injured annually by various accidents. Of the 10 000 000 civilian accidents which occur annually over 330 000 result in death, the great majority of these injuries involve the extremities. As a result of wartime experience by so many of the medical profession it is probable that the emergency treatment of our civilian casualties is better than ever before. However, a strong tendency developed during the war to consider injuries of the extremities even in the absence of damage to the skeletal system as orthopedic cases. Because of this influence often from higher professional authority even well trained general surgeons began to doubt their own capabilities in the management of these cases. As Griswold has properly emphasized, surgery of trauma has tended to be neglected by the teachers and professors in our schools of medicine. Since they have largely been interested in aspects of surgery other than trauma a similar attitude has been developed in the students, interns and residents.

While fractures continue to be cared for on some general surgical services, there is a tendency to group them in the orthopedic or a separate fracture service. If we extrapolate approximately 2 per cent of the teaching centers did not indicate training in the treatment of fractures. While the general surgeon in large city or connected with a group practice may not be required to treat fractures, the opposite is probably true for most general surgeons. Surprisingly enough however in our small survey it was found that only one half of the surgeons were treating fractures. Since the general surgeon is very rarely concerned with complicated orthopedic techniques, it would seem more practical to have a separate fracture service. Such a service could be utilized to mutual advantage in the training program of both general and orthopedic surgeons.

It was generally accepted that urology deserved inclusion in the graduate training program even though it was not provided in one third of the services analyzed. According to the survey of work done by the general surgeons over the country it was not uncommon for them to perform a procedure within this field 100 times of the year if this is the case in which they practiced. Perhaps this emphasis is an exaggeration justified at the expense of their specialties.

Despite the fact that neurosurgery was generally considered outside the scope of the general surgeon, training in this specialty was offered in approximately 60 per cent of the services surveyed. Judging from the analysis of the distribution of the work done by the general surgeons they rarely need for patient in this particular field. The crux of the problem appears to be the furnishing of sufficient training for intelligent management of emergency cases in this field will not unduly prolong the training program.

In general, pediatric surgery was not rated as a specialty and apparently one third of the teaching centers did not provide experience in this field. Since

specifically set aside for this. It can be seen from the foregoing that basic science, general surgery and thoracic surgery were universal features of the training program. The other specialties have not fared so well. For example, approximately 17 per cent of the teaching centers indicated that training was given either in orthopedics or in the management of fractures, or both. Urology was offered in approximately the same number (10 per cent) and neurosurgery by 60 per cent. Experience in pediatric surgery was included in one-half the services, while only 1 per cent provided training in gynecology. Experience in plastic surgery was specifically included in 40 per cent of the services. Rotation in anesthesia and intensive surgery was offered in 30 per cent.

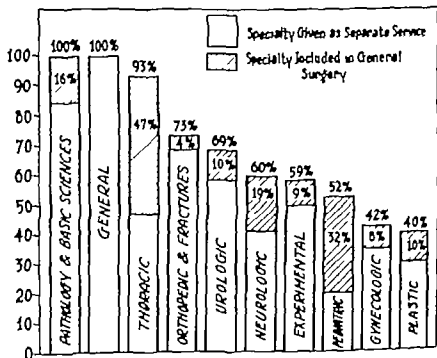


FIGURE 1. Distribution of surgical specialties in forty-eight teaching centers.

It should be noted that the training programs, as they now exist, are not commensurate with the expressed needs of the teachers of surgery and a major institution to not appear to fulfill the needs of the practicing general surgeon. Let us consider the qualitative and valuable.

The position is commonly expressed that the surgeon should open the chest as fearfully as the lightning. The increasing use of the thoracic approach for lesions of the upper gastrointestinal tract makes it mandatory for the surgeon to be thoroughly familiar with the principles of thoracic surgery. Not all of the centers have been able to provide this necessary training.

Treatment of the extremities was invariably regarded as being within the scope of general surgery and it was the opinion of the majority that it is highly desirable for the young general surgeon to receive training in the management of fractures. Mather Cleveland pointed out in a panel discussion on emergency surgery presented before the American Medical Association in June 1947 that almost 8 per cent of our population is injured annually by various accident. Of the 10,000,000 civilian accidents which occur annually over 330,000 result in death, the great majority of these injuries involve the extremities. As a result of wartime experience by so many of the medical profession, it is probable that the emergency treatment of our civilian casualties is better than ever before. However a strong tendency developed during the war to consider injuries of the extremities, even in the absence of damage to the skeletal system as orthopedic cases. Because of this inference often from higher professional authority even well trained general surgeons began to doubt their own capabilities in the management of these cases. As Griswold has properly emphasized, surgery of trauma has tended to be neglected by the teachers and professors in our school of medicine. Since they have largely been interested in aspects of surgery other than trauma a similar attitude has been developed in the students, interns, and residents.

While fractures continue to be cared for on some general surgical services, there is a tendency to group them in the orthopedic or a separate fracture service. However approximately 5 per cent of the teaching centers did not include training in the treatment of fractures. While the general surgeon in a large city or connected with a group practice may not be required to treat fractures the opposite is probably true for most general surgeons. Surprisingly enough however in our small survey it was found that only one-half of the unknown were treating fractures. Since the general surgeon is very rarely concerned with complicated orthopedic techniques, it would seem more practical to have a separate fracture service. Such a service could be utilized to mutual advantage in the training programs of both general and orthopedic surgeons.

It was generally accepted that urology deserved inclusion in the graduate training program even though it was not provided in one third of the services analyzed. According to the survey of work done by the general surgeons over the country it was uncommon for them to perform a procedure within this field, regardless of the size of the city in which they practiced. Perhaps this emphasis on urology is not justified at the expense of other specialties.

Despite the fact that neurosurgery was generally considered outside the scope of the general surgeon, training in this specialty was offered in approximately 60 per cent of the services surveyed. Judging from the analysis of the distribution of the work done by the general surgeons they rarely cared for patients in this particular field. The crux of the problem appears to be the furnishing of sufficient training for intelligent management of emergency cases in this field without unduly prolonging the training program.

In general plastic surgery was not rated as a specialty and apparently one-third of the teaching centers did not provide experience in this field. Sur-



specialty set out for this. It can be seen from the foregoing that basic science, general surgery, and thoracic surgery were universal features of the training program. The other specialties have not fared so well. For example approximately 7 per cent of the teaching centers indicated that training was given either in orthopedic or in the management of fractures, or both. Urology was offered in approximately the same number (10 per cent) and neurosurgery by 60 per cent. Experience in pediatric surgery was included in one-half the services, while only 4 per cent provided training in gynecology. Experience in plastic surgery was specifically included in 40 per cent of the services. Rotation in anesthesia and roentgenology was offered sporadically.

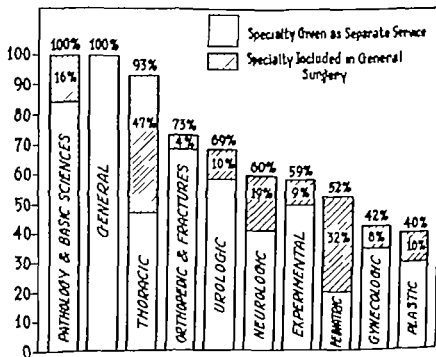


Fig. 1.—Analysis of training programs in general surgery in ten teaching centers.

It should be made clear that the training programs, as they now exist, do considerable violence with the expressed belief that the teachers of surgery in many instances do not appear to fulfill the needs of the practicing general surgeon. Let us consider the specialties involved.

The problem was enormous. It was pointed out that the surgeon should open the chest as frequently as the abdomen. The mere suggestion of the thoracic approach for lesion of the upper gastrointestinal tract made it mandatory for the surgeon to be thoroughly familiar with the principles of thoracic surgery. Nearly all of the centers have been able to provide this necessary training.

The importance of the dual function of such a laboratory in stimulating original contributions and in providing technical experience for the young surgeon in these days of decreasing availability of clinical material is universally recognized.

It is evident from the information gathered from these surveys that there are several problems in the training of the general surgeon which are common to the majority of teaching centers. The most immediate and wide-spread problem continues to be their self imposed obligation to train as many veterans as possible regardless of how far these men had progressed in their graduate training before entering the armed forces. As a result many teaching services have more men in training at the present time than they may have in the near future. Information was available from thirty-eight teaching services as to the number of new appointments in general surgery they plan to make each year. This number ranged from one to as many as thirty in a large private clinic. Almost one half the university teaching services appointed less than four new men a year. Most of them had twelve or more men at the assistant resident level. The majority indicated that approximately two men a year would be eligible for examination by the Board of Surgery.

A second problem has resulted from the various specialties developing their own graduate training programs. As a result, the opportunities for acquainting the young general surgeon with these specialties have steadily diminished. Although the assistant residents may be exchanged between the general surgical service and the various specialties, it frequently happens that they are in such a subordinate position to full time residents that their responsibilities are limited. There are few teaching centers remaining in this country which include many of the specialties as a part of the general surgical service. The chiefs of such services so far have been able to withstand the pressure for decentralization and continue to offer a broad experience in general surgery.

A third problem arises from the preceding one as a result of many of the specialties requiring one or more years of general surgical training. For example the Board of Neurosurgery, Orthopedic Surgery and Plastic Surgery require or will require one or more years of training in general surgery. Furthermore many of the other specialties, because of the great backlog of men desiring specialty training indicate that one or more years training in general surgery will be desirable before they are appointed to that particular service. It is rumored that the Board of Thoracic Surgery now in the process of organization, may require three years of training in general surgery followed by two years of thoracic surgery. This Board, like the Board of Proctology, may require certification in general surgery preliminary to certification in this specialty. Since the average teaching service makes but four new appointments a year or less, it is obvious that there will either be little opportunity for training in general surgery for those entering a specialty or there will be few men available for parallel training in general surgery.

While it is possible at the present time to fill vacancies in the various levels of the training program in general surgery with men of adequate experience and qualifications, this situation will not exist when the backlog of veterans

some of the most important advances in surgery in recent years have been in the surgical correction of disabling congenital anomalies. It might be argued that this field of surgery deserves more emphasis in the training of the general surgeon than is now being given.

The most glaring discrepancy between the actual needs of the practitioner of surgery and what is being offered in the training programs exists in the specialty of gynecology. Nearly two-thirds of the teaching centers surveyed appear to offer no training in this specialty. Since it is commonly combined with obstetrics in a separate department completely staffed by its own residents, it is often impossible for the young surgeon to rotate through this service except by special arrangement. Yet the majority of professors indicated actual experience in gynecology as essential. The opinion was expressed that in these days of radical surgery in the treatment of malignant disease it is impossible to establish a logical barrier between surgery of the abdomen and surgery of the pelvis. Not only was training in gynecology deemed desirable from a diagnostic as well as a technical standpoint, but it was implied that the young general surgeon should develop an appreciation of the nonoperative and physiologic aspects of this field. Certainly a service which trains general surgeons for practice outside the large teaching centers must include a liberal experience in gynecology since our survey shows that the incidence of work in this field ranks second only to gastrointestinal surgery.

An appreciation of the principles of plastic surgery were regarded as desirable although approximately two-thirds of the services did not indicate specific experience in this field. Our survey indicates that practicing surgeons list a surprising amount of work which they consider within the realm of plastic surgery.

It is fair to state that minority of opinion exist that rotation in the various specialties unnecessarily prolongs and dilutes the training program. The proponents of this view believe that short periods of time spent in the specialties result in superficial training and stunting of productive thought. There can be little argument that those teaching clinics concentrating in a particular field are fulfilling an important mission, supplementing those other teaching services which provide all-around background regarded as essential for the general surgeon who might practice in smaller communities. Regardless of the type of graduate training programs offered, a most important quality to develop in a young resident surgeon is an inquisitive and skeptical approach to the problems of surgery including those which believe to be satisfactorily solved.

It is gratifying to note that time in the experimental laboratory was a feature of almost 60 per cent of the training programs. Eight services indicated that at least twelve months in the experimental laboratory was planned for those aspiring to the chief residency. Although only a few months were earmarked for this purpose in some services, it was indicated that the resident staff was encouraged to continue in educational work throughout the period of training. Undoubtedly the handicap of finances and a suitable space interferes with the establishment of experimental laboratories where they are greatly desired.

ground in general surgery who subsequently developed an interest in a special field. A Bonney has pointed out: "Too restricted attention to one subject cramps the outlook, narrows the mind, destroys the sense of proportion, deforms the specialty, and tends in the end to transform it into a cult."

The teachers of surgery in this country can influence the future trend in the graduate training of young surgeons. They must continue to offer opportunities for those interested in an academic career and research. At the same time they should accept the responsibility of training the surgeon to meet the needs of practice. Can it be said that surgery has become so complex that it is no longer possible to educate a man who is safe and competent in the several fields of a general surgeon? Will the medical needs of our country be better served by the apparent trend toward greater specialization? Apparently the majority of teachers of surgery believe that the current inroads of system specialization should be resisted by providing a variety of training for the young general surgeon.

If we are correctly judging postwar trends in the graduate training of general surgeons, concerted action will be necessary by the teachers of surgery to prevent further limitation from their expressed ideal.

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desiring training has been assimilated. It is apparent that the general surgical services will be requested to carry an increasingly heavy load for the specialties. Therefore those in charge of the training programs in general surgery have the bargaining power to insist upon reciprocity with those surgical specialties which they believe offer essential experience for the general surgeon.

Since it is the majority of opinion of the Chiefs of Surgery that a broad training in general surgery is essential before intended specialization, it follows that they would gladly offer this experience whenever possible. They deem early specialization in a narrow field because surgeons trained in this manner are apt to consider the patient in the restricted area of their own specialty to the exclusion of a comprehensive view of the problem in its entirety. Furthermore there is an inherent danger in training specialists without adequate background in general surgery because many of these men may settle in communities where they find that they cannot earn a livelihood by limiting themselves to their field. As a result they expand into general surgery without sufficient training.

It can be seen from the foregoing that a general surgical service has a two-fold obligation to supply the basic surgical training for the surgical specialties, and to furnish the requisite experience for the general surgeon. Some centers are solving the problems we have just discussed in the following manner. After an internship, perhaps of the rotating type, the initial appointment to the general surgical service is a senior internship or junior assistant residency. This service is so organized that a relatively large number of men can be appointed and rotated for short periods through the various specialties. This provides a pool of men to meet the needs of both the general surgical service and the several specialties. Such a service provides broad experience and at the same time fulfills the requirements in general surgery for the several specialty boards. During the following years, an desired exchange between the various specialties and the general surgical service is arranged.

Perhaps one might venture to suggest that a better solution, although one more difficult to accomplish, would be an alteration of the requirement of the surgical specialty boards. Since the various fields of surgery have principles common to all it would seem logical that the three years of fundamental training in general surgery would be equally useful to all.

Perhaps it is not too bold to suggest that some of the specialty boards might liberalize their requirement and recognize three years of general surgical training, and decrease the number of years in specialty training.

The adaptability of the well trained general surgeon was demonstrated in the recent war. Spurling and Churchill have called attention to the fact that the experiences of World War II gave support to the idea that proficiency in specialty following an adequate grounding in general surgery might not take as long as had been previously believed.

It must be accepted that surgical progress has followed the path where eventual concentration in a relatively small field involves greater productivity than is otherwise possible. However, it should not be forgotten that much of the progress in the past has been made by those having a broad back-

**Ileostomy** In the second group even though the colonic disease is quiescent colectomy is proposed, as a means of relieving the patient from a life-long abdominal ileostomy. Some will wish to add that cancer occasionally develops in the retained rectum. About 2 per cent of individual with chronic ulcerative colitis are said to develop carcinoma of the colon or rectum. One further point must be made. So far as we know, there is no necessity to resect more than the mucosa, if any purpose can be served by leaving the other coats.

In polypoid adenomatosis of the colon it is generally agreed (Pugh and Nemeth, and Lockhart Mummery<sup>2</sup>) that most or all of the patients with this condition will ultimately develop carcinoma of the colon unless colectomy is performed. Surgeons have long been tempted to compromise by performing a subtotal colectomy, anastomosing the ileum to sigmoid or rectum, and treating the tumors of the remaining segment with the electrocautery. Lillenthal, Soper, Erdman, and Tom Jones, Lockhart Mummery, Stone and Rankin, have all reported successes by this method. However in many such patients cancer has been reported to develop subsequently. One such patient has been observed<sup>3</sup> at this hospital and at the 1941 meeting of the Society of University Surgeons two patients were reported who developed cancer in remaining segments of the large intestine after partial colectomy for adenomatosis of the colon. There are few times when it is given to a surgeon to say as it is in this condition that he can prevent a cancer which would otherwise surely occur. To leave the rectal segment is a dangerous compromise since despite the removal of most of the colon it is present in the segment which remains that cancer usually develops.<sup>4</sup>

In June, 1947 observations were reported on dogs with a one-stage total colectomy and anal ileostomy with preservation of the sphincter. This procedure has been applied to two patients with ulcerative colitis. A third patient with familial polypoid adenomatosis of the colon, one of five members of his family so afflicted, has had a subtotal colectomy and ileostomy but has not yet had the procedure completed.

#### CASE REPORTS

Case 1 (J. H. H. 15214) — B. G. a 51 year, aged 44 years. H. had developed chronic colitis in 1922, at the age of 16 years. The symptoms continued unabated for four years despite large doses of medical treatment and in hospital treatment elsewhere. H. had eight to ten stools daily (16 blood and pus and occasional tenacious protrusion of blood and pus). H. had lost twenty-four pounds in eight (from 196 to 192) and had severe anorexia.

In J. H. 1928 a terminal ileostomy was performed. The patient's general condition failed to improve. The discharge of blood and pus continued, but had almost constant bloody pus, and the hemoglobin dropped to 49 per cent. The sigmoidoscopic picture was unchanged.

In April, 1940 colectomy was performed as far as the sigmoid which brought out mucous stools. Sections of the bowel (Fig. 1, 2) showed moderate swelling and thickening of the submucosa and atrophy of the mucosa, but no actual ulceration. The perianal area was normal.

Since this report was submitted three more patients have had total colectomy and anal ileostomy for chronic colitis. There has been no death and the results thus far are encouraging.

Johns Hopkins Hospital, Dr. F. Praeger.  
Johns Hopkins Hospital, Dr. D. H. Brown.

## ANAL ILEOSTOMY WITH SPHINCTER PRESERVATION IN PATIENTS REQUIRING TOTAL COLECTOMY FOR BENIGN CONDITIONS

MARK M. RAVITCH, M.D., BALTIMORE, Md.

*(From the Department of Surgery of the Johns Hopkins University and Hospital)*

THE advisability of preserving the anal sphincter in carcinoma of the rectum is currently being discussed more actively than ever before. The procedure presented here may be considered apart from that discussion because it is proposed for nonmalignant disease and because it is the ileum which is brought down through the anal sphincter to the anal skin.

It is clear that in benign conditions requiring total colectomy there is no need for removing the sphincter muscles and it remains to be certain only that a colectomy is required and that satisfactory bowel habit can be established with an anal ileostomy.

Regarding the necessity for total colectomy, I find it required in some cases of ulcerative colitis and in most cases of polypoid adenomatosis of the colon. In severe Hirschsprung's disease a subtotal colectomy has occasionally been performed with an anastomosis of the ileum to the rectal ampulla. In that condition there is no need to excise all of the rectal mucosa.

In chronic nonspecific ulcerative colitis operative treatment is a confession of ignorance and an admission of inadequacy, but at present an ileostomy performed early in the disease is often a lifesaving measure. If early performance of ileostomy one hopes to arrest the disease before the colon has been hopelessly damaged, so that it may subsequently be possible to reanastomose the bowel. This desideratum is not often achieved although in an occasional patient one may be justified in attempting to restore intestinal continuity. However, our interest has been centered in two other groups of patient. In the first group are those patients who after ileostomy still have active disease of the colon with pain and discharge of blood and pus and the threat of perirectal abscesses and fistula. Such patients will be greatly benefited by removal of the diseased colon, and in the past it has been the practice at this hospital to perform a total colectomy, the last stage of which is a peritoneoperineal resection of the rectum. It has been the general experience, as demonstrated again by the patient in Case 1, that a segmental colectomy is inadequate and offers little hope for subsequent restoration of intestinal continuity. The disease is usually most severe in the rectum—the very segment which would be left behind. In the second group are those patients who are apparently well after ileostomy without symptom from the retained colon, but whose disease has progressed so far and produced such extreme changes in the colon that there is no hope of ever restoring intestinal continuity. In the first group with persistent colonic infection the necessity for colectomy is generally conceded and it is proposed merely to modify the operation by providing a continent anal

of the case. The firm discharge as becoming soft and greenish and last being a reasonable normal stool. However the mineralide or soap contained in the P.B. 9 1955 the agentwork due to the 100000 entered again in the operation of trading a hoop held down by submergence. The peritoneal myo is loose and free of adhesion and the greatly dilated ileum passed down through the reconstructed pelvic floor. It met it in the passage from below. The abdominal distention with a great rush of gas and defecation of the bowel. It felt in the lower back on itself below the pelvis floor. Thereafter however cramps in lower were relieved by passing the stool.



Page 2 (continued)      2d. For students 1) previously up to date and completed

[illegible]



He improved slightly after this but continued to pass blood and pain per rectum despite therapy with each new ant biotic which became available. He was finally admitted in January 1947 for completion of colectomy and ileostomy. He was very thin, and still had severe acne. An ileostomy was performed in right M. Dwyer area and very small mucous intails (mucous) at middle medial to the left anterior superior iliac spine (Fig 1). The rectal wall as thickened on roentgenograms (Fig 3) showed remarkably advanced changes with contracted, tubular bowel. Proctectomy showed friable bowel which bled easily and ran with pain. The patient as prepared for operation with sulfonamides by mouth and by irrigation in the rectum.

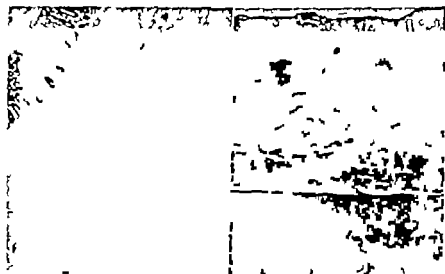


Fig 1  
View of  
stoma of  
ileostomy  
prior to  
operation

of ulcer the time of subtotal enter-  
rectomy, but at many points, espe-  
cially around the stoma, the mucosa is  
in a state of ulceration. The mucosa is  
in a state of ulceration. The mucosa is  
in a state of ulceration.

On Jan 4 1947 the remaining colon was removed and the ileum brought down to the skin in the manner of the ileocecal loop. The ileum was anastomosed to the cecum. The pathologic process had now spread to the cecum. The photograph (Fig 1 B) showed extreme rigidity and ulceration of the mucosa. Only the terminal glandular mucosa remained. The mucosa was heavily infiltrated by inflammatory cells. The submucosa was greatly thickened and the process had now spread to the cecum. The patient showed an old healed ulcer which had completely resorbed mucous continuity. Per iliac, 100,000 units per day given postoperatively. The operation proceeded itself well tolerated. The day after the operation had passed neither fever nor distention.

Miller Abbott tube was passed. He remained completely obstructed until January 21, the eighth day. Some fecal material passed on the perineal dressing. All fluids, including the perineal, had healed closed. For several days liquid feeds and intermittent and without control. As soon as he was started on soft diet on the twelfth day he had violent cramps with variable perianal seepage relieved by remaining motionless. He was kept Miller Abbott tube. Often, after such cramps, back repositioning severe there would be an explosion of fecal discharge. Feb 7 1947 the ileostomy of the patient as he had held back stool for one hour until extreme severe cramps demanded evacuation.

would be felt in the pelvis. Sphincter tone as far as voluntary tightening of the sphincter was rather good. It held it to four stool daily and several at night. Usually he awakened to a stool at night but at times he failed. After discharge from the hospital he began to make rapid improvement. He was learned that by relaxing at stool instead of straining he could evacuate it with and found it necessary to evacuate only after breakfast and supper. When he spent fifteen to twenty minutes on the commode the cramps became less annoying and then he frequently incontinent at night. This tone, as gradually increased. During his stay in the hospital he gained 15 pounds and in January 1918, he weighed 145 pounds, a gain of over sixty pounds since discharge (Fig. 4). Until September 1918 he had a perianal draining because of occasional soiling. By September he was never incontinent day or night and only a soft formed stool a

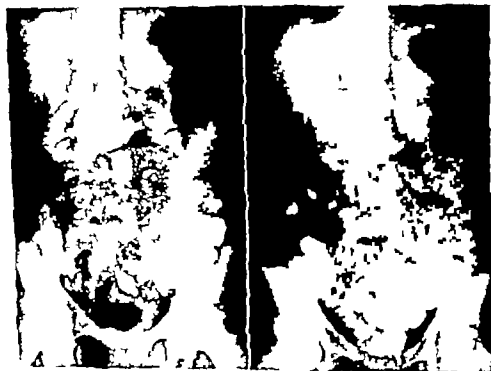


Fig. 5. Roentgenogram of barium meal, August 31, 1917, showing normal haustra. The stomach is not empty. Some of the small bowel has filled with barium. The colon is normal. Fig. 6. Roentgenogram of barium meal, September 1, 1918, showing a more irregular and dilated colon with some narrowing of the lumen.

day and no abdominal cramps. The old scars had disappeared and he found that he had never looked so well. He said he had the typical ulcerative colitis of the type of the colon. He had a hard work and he continued manager of the department of department store. He had a much broader diet than before operation, eating only an extreme of raw fruit. Roentgenogram (Fig. 3) of the gastro-intestinal tract shows complete emptying of the stomach in 4 hours. In which case barium has just reached the distal ileum. The distal ileum (Fig. 6) shown in retrograde injection, enormously dilated. Chromium taken for months with perfect results. The stool next morning and in the next few additional stools from hours or thirty-six hours after operation. There is no evidence of proptosis. He persists dry and sphincter tone is good (Fig.



Fig 2 (Cont.)—D. C. rectosigmoidograms. A Barium enema June 1948 (4 months after subtotal colectomy). The colon is smooth and less distensible than normal. B Barium enema in August 1947. The rectosigmoid is narrow rigid tube.



Fig 3 (Cont.)—D. C. Aug 18, 1947. This has had gained thirty pounds in last three months. (Note the normal thirty pounds.)

**Summary.**—This man, 49 years, known to have had ulcerative colitis since the age of 16 years (1914) had terminal ileostomy performed in 1940. Subtotal colectomy (symptoms from the distal segment persisted) and J ileostomy (colectomy) completed and anal ileostomy performed. Recovery was slow and obstruction more problem than diarrhea. By the fourth month he had satisfactory sphincter control and had begun to gain weight. He gained sixty pounds in eight months, but his former stool did does not suit his mother very well, he has cramps, and full diet and is full of gas. The terminal ileum is greatly dilated.

**Case (J. H. H. 47405).**—A white woman, aged 50 years. The patient's symptoms of ulcerative colitis began when she was 25 years old and progressed steadily until she had lost fifty pounds in eight months. Medical treatment was unsatisfactory. A J ileostomy performed January 1945. Her general condition improved considerably but she continued to have blood-streaked stools and on one occasion required admission for continuous bleeding which had reduced the hemoglobin to 5 (gm). The colon resected (Fig. 8). Sigmoidoscopies continued to show active ulceration. It felt that there was no hope of restoring fecal continence and that since she still has no symptoms from the ileostomy, colectomy should be performed.



Fig. 8. Specimen of colon removed. The colon is greatly dilated.

She was fairly well nourished, weighing 115 pounds. There was a dilated, contracted (fragments removed) (Fig. 9) at the right of the umbilicus below the umbilicus, and in the right lower quadrant there was a red, button-like mass which was small, protruded. The perianal region showed healed scars of the old incisions but no fistula. The rectum was dilated, rigid, and filled with fecal blood. The sigmoid was prepared for operation by distal rectal resection. It felt that the patient had no chance of relief that the anal distal mass was a tumor, and anal resection was done. Three days before operation a nasogastric intubation of jejunum, 1,000 cc. every three hours, began. A operation done.



D

Fig. 1.—D. and B. Box, taken on the run, 1947. The image of the dental arches is visible through the mouth. The image of the dental arches is visible through the mouth. The image of the dental arches is visible through the mouth.



11, 1917 total collection was performed (Fig. 10). The neostomy freed and brought down through the sphincter and the leuco entered the anal. The patient tolerated this extensive procedure very well. A Miller Abbott tube had been passed preoperatively. About the ileostomy and the tip of the tube was below the pelvic floor at conclusion of the operation. She got out of bed and sitting on the fifth day. Liquid stools began to drain on the fifth day and she began to eat on the tenth day. Strychnine was continued parenterally for five days, penicillin for twenty days. By the second week she was eating the cereals and was able to retain the liquid stools for a few minutes. Several cramps appeared at this time and were severe. She could distinguish feces and flatus by the third week. All wounds healed per primam. At three weeks there was no more evidence of the anal stenosis. She had no stooly day. The removal without difficulty and ease of the right iliac fossa and energy are greater than on the left. She was discharged from the hospital on the fourth week. By the fifth week she had normal stools and had no abnormal drainage. The sixth week she had only two stools daily and the eighth day she had one. She had had an abnormal evacuation since returning home.

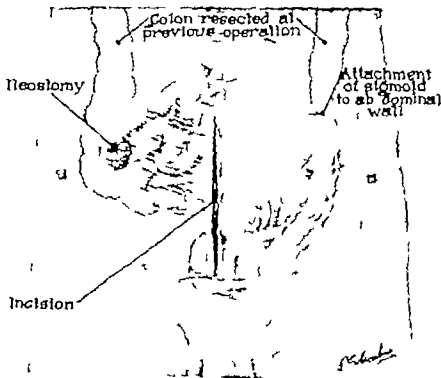


Fig. 11. Case 1. — A. A. Condition (time of operation). Patient had had sigmoid colectomy. The neostomy is in the right lower quadrant. The sigmoid is in the left lower quadrant.

Summary.—The case of J. was a woman who had chronic colitis of eight years duration. Her history in January 1917 did not show the disease in the colon. In December 1917 it was taken a total colectomy and anal anastomosis were performed. She suffered no procedure and. At the time of this report she has made much greater progress than had the first patient. She had a good period of time in that good result expected.



Fig. (Case 3) — \* Intraoral view, right of maxilla, of protruded lower lip (distal) in right lower quadrant.



Fig. (Case 3) — \* Intraoral view, right of maxilla, of protruded lower lip (distal) in right lower quadrant.

11, 1947 total colectomy was performed (Fig 10). The ileostomy was freed and brought down through the sphincter and the hernia sutured to the anus. The patient tolerated this extensive procedure very well. A Milt Abbott tube had been passed preoperatively almost to the ileostomy and the tip of the tube below the pelvic floor at conclusion of the operation. She got out of bed and walking on the fifth day. Liquid feces began to drain on the fifth day and she began to eat on the tenth day. Streptomycin was continued parenterally for five days, penicillin for twenty days. By the second week she was using the commode and was able to retain the liquid stools for a few minutes. Fetal rumps appeared at this time and were severe. She could distinguish feces and flatus by the third week. All wounds healed per primam. At three weeks there was some erosion of the anal mucosa to the anus. She had to stool daily in the commode without difficulty and was eating at night. Her appetite and energy were greater than on admission. She was discharged from the hospital on the fourth week. By the fifth week she had normal stool and had only occasional seepage. The sixth week she had only two stools at night and did not use pads. She had had no incontinence or reactions since returning home.

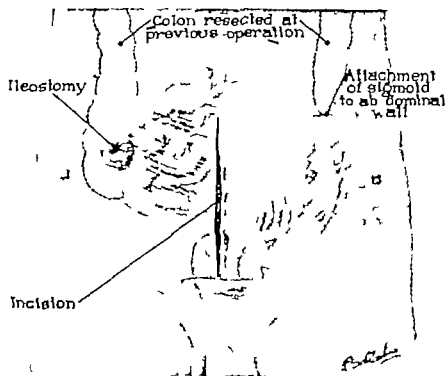


Fig 11. Case 1)—Post-operative condition. Line of operation. Patient had had subtotal colectomy. The ileostomy is in the right lower quadrant. The sigmoid is in the left lower quadrant.

A summary—The patient, a woman of 40 years, had ulcerative colitis of eight years duration. In 1942, she had not first the disease in the colon. In December 1947, a subtotal colectomy and anal hematomectomy were performed. She weathered the procedure well. At the time of her report she had made much greater progress than had the first patient. It took her equal period of time to get good results.



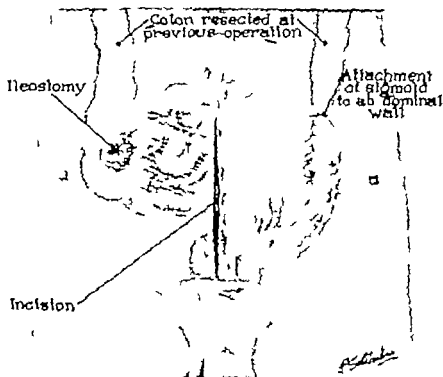


Fig 9 (Case 2)—S R Div with stump, right of midline and prolapsed anal Anus (distal) in high lower quadrant



Fig 10 (Case 2)—S R Div with stump, right of midline and prolapsed anal Anus (distal) in high lower quadrant

11 1947 a total colectomy was performed (Fig 10). The ileostomy was freed and brought down through the sphincter and the ileum returned to the anus. The patient tolerated this extensive procedure very well. A Mike Abbott tube had been passed preoperatively almost to the ileostomy and the tip of the tube was below the pelvic floor at conclusion of the operation. She got out of bed and walking on the fifth day. Liquid feces began to drain on the fifth day and she began to eat on the tenth day. Absorption was a continued preoccupation for five years postoperatively for many weeks. By the second week she was eating the commonest and was able to retain the liquid stool for a few minutes. Intestinal cramps appeared at this time and were severe. She could distinguish feces and flat by the third week. All normal bowel per process. At three weeks there was some evidence of the local anastomosis at the anus. She had a stool a day. The commonest about 4 stools and one to a half. Her appetite and energy are greater than on admission. She was discharged from the hospital on the fourth week. By the fifth week she had an normal stools and had only occasional cramps. The sixth week she had only two stools a day, none at night and did not have gas. She had had no loosest stool evacuations since admission home.



The 11 Cam 11 F-4s received a time of operation almost 100 percent. The patient had had 100 percent of the 11

A memory - The 10 cases of H. virus who had ulcers at colitis 8 eight years  
Jaramila Thrombosis in January 1 (I did not affect the disease in the colon in December  
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procedure in July. At the time of this report who is made much greater progress than  
has the first patient in the trial of equal period of time as that good result  
expected.

## OPERATIVE PROCEDURE

Preoperative preparation consists in the oral administration of streptomycin or of sulfamuxidine or sulfathiazidine. The large bowel is daily irrigated with a solution of one of these agents, and after each irrigation a concentrated suspension of the same drug is instilled in the colon. Before operation an indwelling intestinal tube is passed to the terminal ileum.

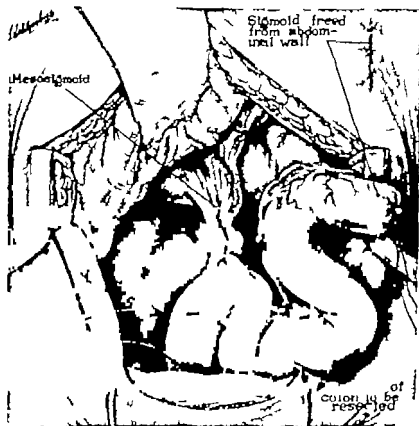


Fig. 12 (Cont.)—B. Mobilization of cecum. The entire sigmoid cannot be placed under the peritoneal floor. The cecum is freed.

The colonic segment (in Case 1 the sigmoid and rectum, in Case 2 the entire colon and two feet of terminal ileum) is freed and resected (Figs 11 and 12) so that only a short stump of rectum is left in the pelvis. This segment must be completely liberated down to the mesocolic pelvic diaphragm. The colon in patients with ulcerative colitis is so rigid and thick-walled that in every case the distal stump is not feasible. I have merely inserted the bowel with the cautery between clamps and tied off the rectal stump with heavy braided silk.

The ilium is then fixed to the abdominal wall (Fig. 13) and tied with the same heavy braided silk. In both instances it was apparent that the ileum would reach through the anus. A little extra length was obtained by cutting the edge of the mesentery without sacrificing any vessels. With the ileum pressed down to the bottom of the pelvis, the anterior surface of the ileum is then marked with a silk suture at the level at which the bowel should be attached to

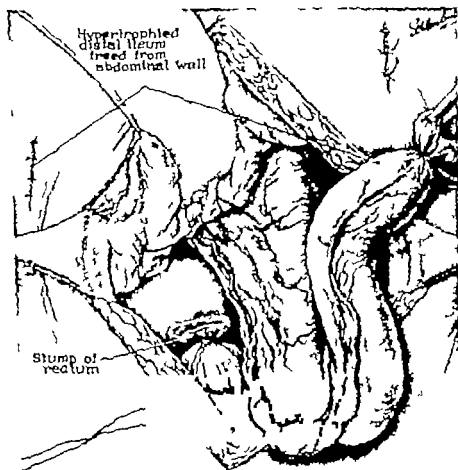


Fig. 13. C = 1. II. The ileum is then freed from the abdominal wall. II. The rectum has been dissected as shown to be in position and is inserted.

the pelvic peritoneum (Fig. 14). This will minimize the likelihood of rotation of the bowel and will ensure one living normal ileum beneath the pelvic floor for the anal anastomosis. The peritoneal floor is then repaired, turning the peritoneal flaps to the right side of the ilial mesentery so that the bowel will sit to the left side of the mesentery (Fig. 15). Care is taken to suture no more than 1 centimeter of the bowel circumference so as not to prevent stenosis of the bowel.



Fig. 1 (Case 1).—R. O. The ileum is tied to the rectal stump. Note marking suture on ileum to denote anterior surface, and level of attachment to pelvic peritoneum.

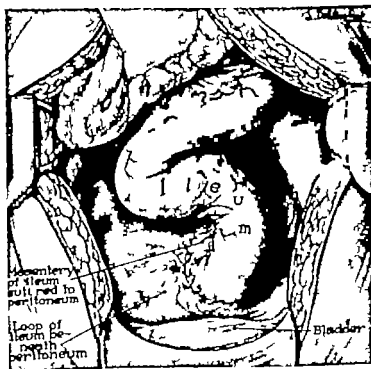


Fig. 11 (Case 1).—R. O. The pelvic peritoneum is repaired. Sutures are tucked in the bowel for only two-thirds of circumference to prevent constriction, other sutures being taken as necessary.

The abdominal wounds are closed and the patient placed in the lithotomy position. The anal margins are grasped with Allis clips and a circular incision is made in the mucocutaneous junction (Fig. 16). The freed edges of the thin tube of mucosa and submucosa which is now dissected up are held with curved clamps and dissection is continued with small curved scissors. The bowel is friable and must be handled gently. The cuff of mucosa and submucosa

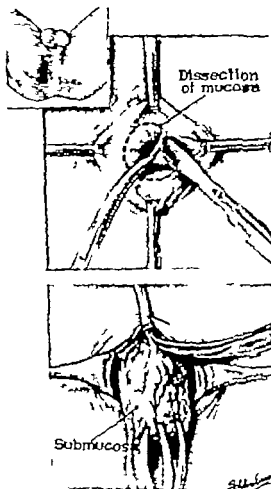


FIG. 16. Case 1.—B. G. Lithotomy position. Dissection of cuff of rectal mucosa and submucosa beneath mucocutaneous junction. External and internal sphincter are unharmed.

is dissected up for two to three inches, then when the outer muscular coats of rectum are cut through (Fig. 1 A) the pelvis is reached. Continuation of this incision circularly frees the rectum entirely. The rectum and attached ileum can then be delivered (Fig. 1 B). The ileum is sutured in three layers. The first, of 0000 catgut is a continuous suture between ileum and the everted muscular coat of rectum (Fig. 1 B). The second, of interrupted sutures of the

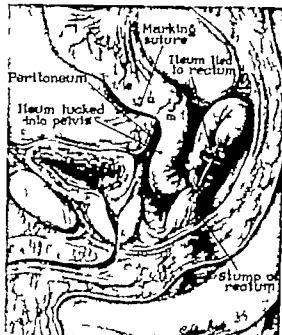


Fig. 2 (Case 1)—P. O. The ileum is tied to the rectal stump. Note marking suture on ileum to denote anterior surface and level of tuckup into pelvic peritoneum.

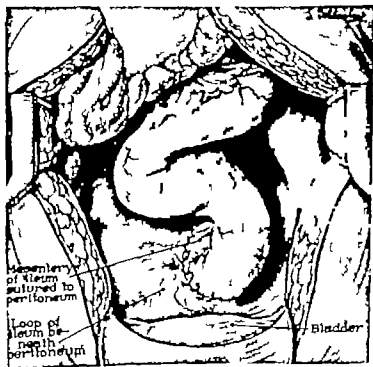


Fig. 3 (Case 1)—P. O. The pelvic peritoneum is repaired. Sutures are stitched to the bowel for only two-thirds of circumference to prevent constriction, other sutures taken in mesentery.

The abdominal wounds are closed and the patient placed in the lithotomy position. The anal margins are grasped with Allis clips and a circular incision is made in the mucocutaneous junction (Fig. 16). The freed edges of the thin tube of mucosa and submucosa which is now dissected up are held with curved clamps and dissection is continued with small curved scissors. The bowel is friable and must be handled gently. The cuff of mucosa and submucosa

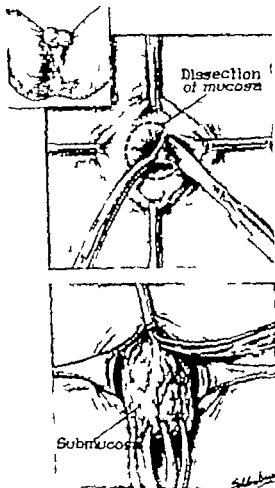


FIG. 1 (Case 1) — (A) Lithotomy position. Dissection of cuff of rectal mucosa and submucosa. (B) Rectum is not injured. External and internal sphincter are uninjured.

is dissected up for two to three inches, then when the outer muscular coat of rectum are cut through (Fig. 17 A) the pelvis is not held. Continuation of this incision circularly frees the rectum entirely. The rectum and attached ileum can then be delivered (Fig. 1 B). The ileum is sutured in three layers. The first of 0000 catgut is a continuous suture between ileum and the everted muscular coat of rectum (Fig. 17 B). The second, interrupted sutures of the



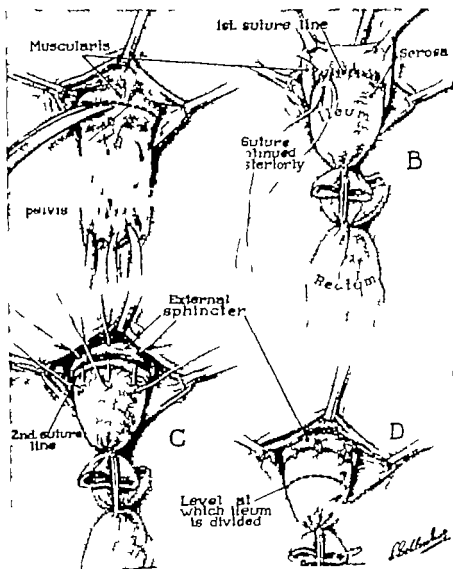
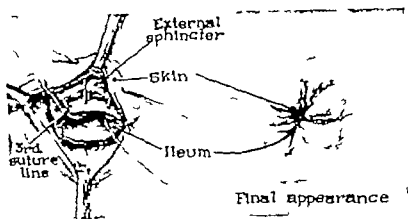


Fig. 7 (Pl. 1—2)  
 shows in which the outer  
 rectum is divided. The rectum is  
 shown partially resected.  
 (Note has been permitted  
 to be transected)

*Ballou*

same material took the ileum & the external sphincter (Fig 1 C) after the first suture line has been permitted to retract. The ileum is then transected (Fig 1 D) so as to reach just to the skin edge to which it is fixed with a few interrupted sutures of silk (Fig 18) for the third suture line.



—The suture line — is of silk between full thickness of ileum and full thickness of skin. No drainage are employed.

#### DISCUSSION

The condition of these two patients is an encouragement to continue the use of this procedure in the relief of patients who must have a permanent ileostomy. Neither in continence nor excitation of the skin has been a problem. Complete flange re-continence and good sphincter tone are gradually regained after operation. The perianal skin in both patients smarted for one or two weeks but have become excoriated. Both of the patients commented within the first month that for the first time since the original ileostomy the stools had taken on the usual appearance of feces. Both patients now have soft formed stools on a regular basis. The first patient required kaopectate for some time. The second patient whose course throughout was much smoother did not require any such agent. Both patients have a defecate urge which they say is a sense of lower abdominal fullness. They are able to distinguish between flatus and feces and can permit the escape of flatus at will.

Nissen has drawn our attention to the fact that in 1932 at a meeting of the Berlin Surgical Society he presented a boy who was stated in the proceedings of the Society to have had a total colectomy and ileo-anal anastomosis for polypoid adenomatosis of the colon. Nissen operating through a sacral approach apparently used the Hochstetzer pull through procedure bringing a bulbous barreled loop of ileum through the sphincter. Wangensteen<sup>11</sup> has operated on a woman for ulcerative colitis, ileitis, subtotal colectomy and anastomosed the ileum to the terminal rectum with a satisfactory result. In another patient he performed a total colectomy with a Hochstetzer pull through with a result which he felt to be unsatisfactory. Babcock<sup>12</sup> stated that in his

experiences total colectomy for ulcerative colitis with some type of pull-through had been unsatisfactory.

The method described here does not injure the external sphincter and preserves the internal sphincter and the attachment of the muscular coats of the rectum to the levator ani muscle. It may be that these features will contribute to a greater measure of success than has been achieved in the past. Simultaneous dissection from above and below as done by Wauershtein,<sup>11</sup> Morgan<sup>12</sup> and Lloyd Davies<sup>13</sup> might have definite advantages. Such a method would permit one to determine with greater precision the level at which the ileum should be sutured to the pelvic peritoneum.

The dilatation of the ileum is to be expected, for to place a continent sphincter at the end of the ileum is to produce a complete, if intermittent, intestinal obstruction. These patients suffered agonizing cramps during the period of dilatation of the ileum, but the first patient has been free from cramps since the fourth month, and the second patient's cramps ceased by the fifth week. Similar dilatation of the ileum, and for the same reason, occurs after the all but total colectomy for Hirschsprung's disease in which only the rectal ampulla has been left for anastomosis to the ileum. Two young patients had an all but total colectomy performed at the Johns Hopkins Hospital, three and four years ago, for Hirschsprung's disease. Both those patients are vigorous and well and in both the ileum is hugely dilated. This dilatation is not a disadvantage but a necessity.

It should be pointed out that the two patients with ulcerative colitis here reported had had the ileostomies for eight years and three years, respectively. In both the terminal ileum was already thickened, dilated, and hypertrophied before operation, although much less than subsequently. In a third patient with familial adenomatosis of the colon it was intended to perform the entire procedure at the very first operation but the patient's condition caused the procedure to be stopped when only the ileostomy and subtotal colectomy had been completed. The second stage has not yet been performed. In any case it may well be that a period of at least several months should be allowed for adjustment to the ileostomy before completion of this operative procedure.

#### SUMMARY

1. An operation is described for the preservation of a continent sphincter in the performance of an anal ileostomy after total colectomy.

2. This procedure is advised in patients requiring total colectomy for benign lesions—specifically chronic ulcerative colitis and polypoid adenomatosis of the colon.

3. Two patients with ulcerative colitis are presented in whom this operation was successfully performed.

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## POLYPOSIS (ADENOMATOSIS) OF THE COLON

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DANIEL P. SCHAUBER, M.D.† CHICAGO, ILL.

POLYPOIDS of the colon occurring either singly or in small numbers are common but polyposis (adenomatosis) is relatively rare. The condition is of particular interest because of its familial and congenital aspects, the diffuse involvement of the colon and the marked tendency to malignant change at an early age. It is important that polyposis be recognized as a clinical entity apart from the general subject of polyps and carcinoma of the colon because of the special problems it presents in diagnosis and treatment.

In the management of polyposis, the segment of colon which should be removed first, the extent and type of resection, the amount of bowel that may be preserved, the number of operative stages to be employed and the question of the use of cautery are important variables. To decide upon the procedure best suited to the individual, it is necessary to make accurate preoperative studies of the general condition of the patient and of the location, extent, completeness, and character of the lesions in the bowel. It is equally essential to the proper management of a patient with polyposis that the surgeon be aware of certain facts concerning the pathology, genesis, and behavior of the disease. To this end an historical review concerning those phases of the disease will be presented in some detail. This review will be followed by a description of the experience of surgeons in the operative management of polyposis since 1930. The year 1930 is selected because a review of the literature makes it apparent that most of the improvements in surgical management have been made since that time. It is important to recognize that surgery has become wide in scope and that in the latter part of the reported period has use of the many therapeutic measures

seven new  
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studies

and in the present-day can justify the disease as a clinical management

### HISTORICAL REVIEW

Little has been added to our knowledge of the pathogenesis and description of the pathology of polyposis of the colon since the last review of the literature made by Cuthbert Dukes<sup>1</sup> in 1930. In this review we assembled the contributions which have made possible the modern concept of the disease. Dukes commented on the terminology, unraveled points of confusion with regard to diseases which resemble polyposis, and delineated the lesions of the disease. It is so noted that they lessens considerable emphasis in the form of a final quotation.

*Terminology*—I quote from Dukes: "The condition of multiple polypoid growths has been described under many different names, such as disseminated

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polyp (Cripps, 1882) multiple adenomas (Whitehead 1884) multiple polyp (Bleekerstein 1890) and multiple papillomata (Dalton, 1893). Other less commonly employed designation have been multiple adenomatosis and multiple polyposis. Fortunately it is not necessary to be guided in our choice of a name by question of priority because none of the earlier descriptions was in any way complete and some contained confusing errors. The reasons for deciding to call the disease by the short and easily pronounceable name polyposis are that this term was used as early as any, it is an accurate description of the condition and polyposis intestini is the recognized label for the disease in every language other than English.

*Distinction Between a Polyposis and Polyp Secondary to Inflammatory Disease*—It is difficult to establish the identity of the first author to recognize polyposis as a disease entity because of the confusion which existed in the eighteenth and nineteenth centuries between primary polyposis and polyposis secondary to inflammatory disease. The tendency to confuse polyposis and polyposis secondary to inflammation was recognized by Woodward in 1861 who suggested the name pseudopolyposis for polypoid growth secondary to ulcerative colitis. Dukes stated that the cases of Meusel (1791) Lebert (1861) and Luschka (1861) collected by Virchow (1863) were reported with a case of his own as examples of the secondary type to which Virchow applied the term colitis polyposa. In a footnote, Dukes added that in the light of subsequent knowledge it is improbable that Virchow's case had the same pathology as the others, indicating that the cases of Meusel, Lebert and Luschka may have been examples of polyposis. Luschka's case was that of a woman, aged 30 years in whom the colon is described as having contained thousands of polyps. Mayo and Wakefield stated that this is the most convincing description of polyposis made by any early writer.

Even today inflammatory colitis and polyposis are occasionally confused clinically and pathologically in cases with long-standing involvement. Secondary inflammatory colitis due to secondary invading organisms may be superimposed upon long-standing primary polyposis, and a lesion may be periplasia with malignant change may occur in polyps which arise in the presence of long-standing inflammatory disease such as in ulcerative colitis or amoebic dysentery. Either circumstance may give rise to identical symptoms. In most instances careful study utilizing recent diagnostic criteria makes possible the distinction between the two conditions.

*Distinction Between Polypoid and Polyp Occurring Either Singly or in Small Numbers*—The third and most common form of polyp encountered at those occurring singly or in small numbers in children or adults. Dukes stated that these are best described under the name of papilloma or adenoma. According to Dukes, although this (1901) was the first textbook writers to differentiate polypoid from polypoid papilloma and adenoma it is not possible to determine the time that polypoid was recognized as an entity.

*Recognition of the Familial Inherited Polypoid and Congenital Polypoid*—The fundamental concept of familial and congenital polyposis was recognized when W. Harrison Cripps in 1882 reported two cases occurring in brother and sister

Many similar case reports followed, and one may refer to Dukes for papers giving the details of familial history of cases and for a discussion of the hereditary factor. Polypoma is an example of gene mutation transmitted by both sexes, and appearing in succeeding generations as Mendelian dominants or recessives. For this reason the disease may appear in every generation of one family and it may not develop for many generations in another. The appearance of polyps is most frequent in the second, third, and fourth decades of life with the peak of incidence at about 30 years of age. An excellent view of the familial and genealogic aspect of the disease is afforded in the article by Lockhart Mummery and Dukes.

*Tendency to Malignant Change*—Handford in 1890 described a case of intestinal polypoids in a woman aged 34 years who died of cancer of the rectum. Dukes stated that the significance of this observation was emphasized a few years later by the masterly review of the disease by Hauser in 1893, and since this date almost every writer on polypoids has drawn attention to the frequency with which it is associated with carcinoma. For the histopathologic characteristics of polyps Fitzgibbon and Rankin made an excellent review and established a classification of interest to the surgeon.

#### REVIEW OF SURGICAL MANAGEMENT SINCE 1930

A principal purpose of this paper is to examine various methods used in the surgical treatment of polypoids. In 1927 J. H. Saint<sup>1</sup> reviewed the literature on polypoid in the *British Journal of Surgery*. In 1934 Lockhart Mummery stated that he had performed the first colectomy for this condition in 1918 and had, in all, done four complete colectomies for the disease. He had, however, removed the rectum in only one case, preferring fulguration of the lower segment as a method of choice unless cancer was present.

Reports of experiences of American surgeons begin about 1930. Tabulation of this experience from the material recorded in American literature has not been made. Hitherto the published data has consisted of groups of case reports from individual clinics, usually accompanied by illustrations and descriptions of preferred techniques and programs of procedure for the most part based upon sound surgical principles. There is a natural tendency on the part of a surgeon, as a rare case is encountered, to apply a given procedure suggested by a publication to the management of a case rather than to vary the approach or modify it in order to suit the individual requirements.

In the following review only cases in which operations were performed on the large intestine in attempts at cure are reported. Reports on patients who died before attempts at resection were made are not included. Also articles which do not give individual case reports are excluded because of the lack of data necessary for analysis.

In 1931 Rankin reported three cases of polypoid in which total removal of the large bowel and rectum was done in three stages—ileostomy, colectomy, and posterior or abdominoperineal resection, in that order. In 1933 three cases were added, treatment in one being the same as in the first three and treatment in the other two being by colectomy and ileosigmoidostomy after ileostomy.

and fulguration of the lower segment. Abstracts of these case reports are as follows:

CASE 1—(1) Ileostomy was performed, with ( ) colectomy of the rectum (7 months later) and (2) posterior resection of the rectal stump (1 week later). The interval between stages (1) and ( ) was  $\frac{1}{2}$  months. Carcinoma of the rectum was present in the initial biopsy material as well as in the removed rectal segment. The patient died 11 months after the final operation. The cause of death was not given.

CASE 2—(1) Ileostomy was followed by ( ) colectomy of rectal stump (3 months later) and (2) posterior resection of the rectal stump (1 week later). The interval was  $\frac{1}{2}$  months. Carcinoma of the rectum was shown on biopsy before treatment was begun and two carcinomas were found in the rectal specimen. The patient was living and well 3 years later.

CASE 3—(1) Ileostomy was followed by ( ) colectomy of the rectosigmoid (4 $\frac{1}{2}$  months later) and (2) combined abdominoperineal resection (6 weeks later). The interval was 6 months. No carcinoma was demonstrated; the patient recovered satisfactorily.

CASE 4—The patient was operated upon in three stages: (1) ileostomy ( ) colectomy of the lower third of the sigmoid (6 months later) and (2) combined abdominoperineal resection of the rectum and anus (3 months later). The interval between the first and third stages was 9 months. Carcinoma was not demonstrated. The patient was well one year later.

CASE 5—The patient was treated as follows: (1) ileostomy ( ) colectomy of the mid sigmoid (2 $\frac{1}{2}$  months later), (2) fulguration of the lower segment (because the polyps were not so diffuse as in the other cases), and (3) lateral anastomosis between the ileum and lower segment (11 months later). The interval between the first and fourth stages was 15 months. No carcinoma was demonstrated. The patient was well two years later.

CASE 6—In this patient surgery and fulguration were combined. First ileostomy was performed, with fulguration of every thickened polyp 6 months later and colectomy to the sigmoidal area 6 months later. Completion of the fulguration was planned, but death occurred on the eighth postoperative day clinically due to peritonitis and pulmonary embolism. This complication precluded a most satisfactory closure of rectosigmoid stump thickened with polyps.

In 1936 Mayo and Wakefield described a new operative technique employed in two cases of polyposis. This treatment consisted of the following steps: (1) fulguration of the polyps in the rectum and lower sigmoid segment; (2) right colectomy and ileosigmoidostomy; (3) left colectomy leaving a sigmoid colon above the site of the ileosigmoidostomy; (4) fulguration from above; and (5) closure of the colonotomy. The first patient was well 18 months after operation. Their second patient developed acute small bowel obstruction after the second stage and died two days after laparotomy and release of obstruction. No carcinoma was demonstrated; the intervals from stage to stage were not given.

Miller and Sweet (1937) reported on 16 patients in each of whom a combined abdominoperineal resection was followed by total colectomy and establishment of an ileostomy. One patient (Case 1) was treated by (1) combined abdominoperineal resection and ( ) resection of remainder of colon with ileostomy. A adenocarcinoma with regional node metastases was found in the specimen removed in the first stage. There was an interval of three months between stages. The patient was well three years later. The second patient



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hospital with obstruction were relieved by Miller Abbott tube and irrigation and drainage of left pelvic hernia on each occasion. (4) Colectomy & the site of the anastomosis was performed 1 yr. after the first operation. The patient had early recurrence of carcinoma on rectal examination.

Pugh and Nesselrod<sup>12</sup> reported two operated cases with recovery. In one case three stages were employed effecting (1) ileostomy (2) colectomy (two months later) and (3) combined abdominoperineal resection of the remaining segment (three months later). Four months intervened between the first and last stages. In the second case all adenomas from the pectineal line to the pelvic sigmoid were fulgurated, following which ileosigmoidostomy was performed. The intervening segment was resected at a second operation three months later. No malignancy was demonstrated in either case.

Wilensky<sup>13</sup> reported one case in which total colectomy and resection of the rectum and anus were accomplished successfully in three stages—right colectomy, left colectomy and abdominoperineal resection of the rectum and anus.

In 1941 Hupfyll<sup>14</sup> reported three cases in which operation was performed on the colon.

(Case 1)—Treatment was as follows: (1) Fulguration on five occasions during the last of which the sigmoid was perforated and treated by laparotomy. (2) Seven months later & laparotomy the sigmoid opened, polyps were fulgurated, and ileosigmoidostomy was done. (3) Right colectomy performed 4 weeks later. (4) Two months later the left colon and sigmoid were removed, down to 3 cm. below the anastomosis. (5) During the next 3 months polyps were fulgurated through the sigmoid colostomy on four occasions. (6) The sigmoidostomy was closed 18 months after treatment was begun. Nine months later stricture occurred requiring laparotomy. (7) Resection of the remaining sigmoid and upper rectum was done six months later because of the presence of numerous polyps and the stricture implanted into the rectal stump. Pathologic examination showed malignant degeneration in polyp removed with the upper rectal segment. In July 1941 diarrhea recurred and in August, 1941 five years after initial treatment began, dilatation of the lower rectal segment required relief obstruction due to circumferential constriction resulting from fulguration of the stricture. Biopsy in October 1941 revealed carcinoma in the rectum. (8) A combined abdominoperineal resection was then done and the patient died 8 months later.

(Case 2)—Treatment as follows: (1) Fulguration of the rectum and rectosigmoid for distance of 10 cm. over period of 8 months with delay in treatment for 3 months because of pulmonary tuberculosis and (2) laparotomy with opening of the ileosigmoid fulguration of polyps and resection of the sigmoidostomy. (3) Right colectomy was performed 6 weeks later. (4) Left colectomy done & the anastomosis followed 8 weeks later. (5) The remaining sigmoid removed with ileoproctostomy 8 months later. The patient was alive 5 years after the last operation.

(Case 3)—Treatment as follows: (1) Cecostomy was performed for obstruction in the sigmoid due to carcinoma. Abdominoperineal resection & sigmoid colostomy followed. Three areas of malignancy were demonstrated in the specimen. Roentgenologic examination revealed numerous polyps throughout the remaining colon. The patient returned 2½ years later with extensive neoplastic process involving the left colonoscopy and the abdominal wall for which (2) complete colectomy was performed.

Garne (1847) reported two patients treated by fulguration, colectomy and ileoproctostomy.

(Case 4)—Treatment as follows: (1) A transverse colectomy was followed in (2) Siles type of resection for carcinoma of the sigmoid (done elsewhere). (3) A one stage

was treated dentically with an interval of one month between stages. In a leucostoma grade 1 from an adenoma in the rectum another in the lower sigmoid, and a third carcinoma in the colon were removed at the second stage. The patient was living and well seven years later.

Scarborough in 1937 reported one patient treated by (1) ileostomy (2) abdominal perineal resection of the left colon rectum and anus (four months later) and (3) right and transverse colectomy (1 month later). Biopsy of the rectum for carcinoma before ileostomy was positive. The interval between the first and last stages was six months. The patient was well three years after operation.

In 1939 T. E. Jones reported a single case with repeated fulguration of the lower segment extending over the period from 1926 to 1930. Total colectomy and ileosigmoidostomy were then performed. The patient died two years later from endometrial metastases.

In 1944 H. Kuman reported one patient who had been treated by (1) fulguration of some 227 polyps in a lesion of 1 inches in the low segment and (2) total colectomy and ileosigmoidostomy in one stage (three months later). No carcinoma was demonstrated. The patient was alive and well twelve years later.

In 1945 operated cases were reported by Laker, Pfeiffer and Patterson, Pugh and Neselrod, and Wilensky.

In one of Laker's two patients there were recurrent carcinomas, three removed by combined abdominal perineal resection, with colectomy and ileostomy later osteoplasty at the time of the report. In the second patient (with fewer polyps in the rectum and no evidence of carcinoma) (1) fulguration was followed by (2) colectomy and ileosigmoidostomy and (3) fulguration of recurrent polyps. The patient was alive and well ten years later.

Pfeiffer and Patterson reported 11 cases with the technique employed and the operative results as follows:

Case 1—(1) Fulguration of the rectum and sigmoid in week intervals for 2 months at another time was followed by (2) ileosigmoidostomy because of hatred of symptoms and patient refusal of surgery. (3) Ileosigmoidostomy and colectomy were performed, but 14 inches of cecum are left because of technical difficulties. (4) Fulguration of polyps in cecum followed by (5) ileosigmoidostomy 1 year later. The patient is living less than 1 year postoperatively.

Case 2—(1) Fulguration, completed after 3 months interval, performed (deliberately uncooperative patient). (2) Fulguration began 7 months later (delaying is due to lack of cooperation). (3) Laparotomy 3 weeks later revealed uncooperability due to extension of carcinoma of the rectosigmoid. A patient removed as low as possible and the patient died on the fourth postoperative day.

Case 3—The stages were followed: (1) first fulguration every 4 weeks for 1 month, (2) ileosigmoidostomy (3) colectomy done by anastomosis at four months after initial fulguration. Less than 1 year after the last fulguration, less than 1 year postoperatively.

Case 4—(1) Removal of adenoma of sigmoid with sigmoid colectomy and turning in the distal stump was followed by (2) repeated fulgurations of rectum and blood sigmoid segment and (3) ileosigmoidostomy 3 months after initial resection. Two returns to the

It and the temperature pulse and respiration were normal. No abnormalities were noted on examination of the abdomen. The red blood cell count 1,500,000 hemoglobin 9 Gm; and repeated stool examinations were from 1 to 4 plus positive to guaiac test. An occasional stool contained red blood.

A barium enema with air contrast media performed on the day after admission revealed numerous oval filling defect throughout the region of the transverse and descending colon. There was also deformity at the splenic flexure.

On proctoscopic examination numerous sessile and ulcerated polypoid lesions were found on the posterior wall of the rectum 1 to 2 inches from the anal ring. The lesions were about 10 mm in diameter and were interpreted as being malignant on proctoscopic inspection and after microscopic examination.

The patient was placed on low residue diet. Stools B and C were given, the hemoglobin and red blood cell count were brought to normal levels with 10 transfusions of whole blood.



FIG. 1—L. H. Specimen removed at second operation.

A second operation on July 17, 1941, laparotomy performed through long left rectus abdominis incision. Inspection of the bowel confirmed the presence of numerous lesions in the region of the splenic flexure, middle portion of the transverse colon, and numerous of large nodules in the regional mesentery of the left half of the transverse colon and the splenic flexure. There was no evidence of extension of masses beyond the regional mesentery. The rectum and sigmoid colon revealed no pathology. A resection of the transverse colon including the hepatic flexure and all of the left colon, rectum, and anus was then done with the left internal iliac vessels to the abdominal aorta. A colostomy was performed at the level of the ascending colon just below the hepatic flexure. The postoperative course unremarkable and the patient was discharged from the hospital one month after operation.

**Pathology**—Examination of the specimen revealed numerous carcinomas of the splenic flexure. Carcinoma of the rectum just below the rectosigmoid junction, previously identified on proctoscopic examination, and the lesion seen just to the left of the middle of the transverse colon. In addition, there were numerous small polyps arising from 0.5 to 1.0 cm diameter extending from the rectosigmoid junction to the left and including the left colon and the left half of the transverse colon. There were no polyps in the right half of the transverse colon.

colectomy and ileoproctostomy were performed after (4) fulgurating polyps of the rectum 3 months later. The patient well  $\frac{1}{2}$  yr later.

CASE 2.—Treatment (1) 1 repeat fulguration of polyp of the rectum and (2) transabdominal removal of polyp over period of two years in other hospital. (3) Colectomy and ileostomy performed after (4) 2nd fulgurating rectal polyp. Early malignancy was found in the rectum. The patient was ill 15 months after the 1st operation.

Mandel and Root (194) reported a case of polyposis in which there was prolapse of the rectum. The patient was treated as follows: (1) a loop transverse colectomy (2) right colectomy and ileotransverse colostomy (3 weeks later) (3) pelvic resection of the rectosigmoid preserving sphincter function by attaching the sigmoid to the anal sphincter (9 days later) and (4) closure of transverse colostomy stoma (4 weeks later). No mention was made of the method employed to remove polyps in the segment of transverse descending colon which was allowed to remain. Carcinoma was demonstrated in the appendix and cecum. The patient was living at the time of the report 10 months after operation.

In addition to these summaries seven recent and consecutive cases of polyposis in which the patient was treated by resection of the colon will be presented. Four of these patients were operated upon by one of us (PIII) and three by the other (DPS). In one patient sphincter function was preserved by combining the use of cauterization with colectomy. Three patients were treated by total ablation of the large bowel in stage operations, after unsuccessful attempts were made to preserve segment of the colon in 2 of these. In one patient ileostomy, total colectomy and proximal resection of the rectum and anus were performed in one stage. In another patient total removal of the large bowel except for the cecum was made. The seventh case had only abdominoperineal resection of the rectum and sigmoid and is presented as a questionable case of polyposis. All seven patients survived surgery and are now living.

#### CASE REPORTS

##### CASE 1.—

HENRY—L. K. Late in life was aged 50 years, admitted to the surgical service of the Cleveland General Hospital on July 1, 1941, with chief complaint of diarrhea and bloody stool of one year's duration. For two months prior to admission there had been episodes of abdominal distention and left lower quadrant discomfort.

The patient had been in good health until one year before admission, he had then developed and increased frequency of four or five stools daily and increased tinged with red blood. Ten months before admission he had developed feelings of distention and soreness in the left lower quadrant which periodically recurred and disappeared throughout the day.

Since the onset of the symptoms one year before general health had deteriorated considerably with weight loss of twenty three pounds (175 to 152 pounds), increasing feelings of fatigue and weakness and dyspepsia which was brought on by moderate exercise. The only family history obtainable was that his mother had died of cancer of the intestine about twenty years earlier, he exact etiology of which was unknown.

Preoperational Study and Preparation.—Physical examination revealed pale, young man, he appeared to be undernourished and underweight. He did not appear to be acutely



Fig. 2—J. R. Results of biopsy of the colon. (A) large polypoid lesion; (B) smaller polypoid lesion.

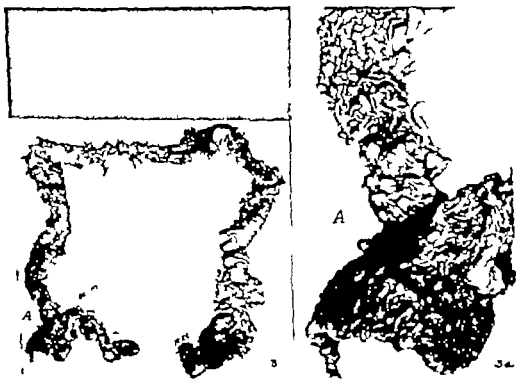


Fig. 3—J. R. Specimens removed by colonoscopy. (A) large polypoid lesion; (B) smaller polypoid lesion; (C) large polypoid lesion.

**Follow-up Study**—The patient was again admitted to the hospital on April 1, 1946 (4 years later) with history of having experienced difficulty with control of the colonostomy. The stools had become watery and loose and an offensive odor had developed which prevented him from gaining employment. There had been occasional appearances of blood with the stool and the patient had lost about ten pounds in weight. Polyps stained the mucosa of the colonostomy. On April 29, 1946, through transverse incision, the remaining portion of the colon and 6 inches of terminal ileum were resected and an ileostomy was performed.

Examination of the specimen removed at operation (Fig. 1) revealed the presence of numerous sessile knob-shaped polyps varying in size from 0.5 to 1.0 cm. in diameter and elevated about 0.3 cm. above the general level of the mucosa. The intervening mucosa was normal in appearance and there was no gross or microscopic evidence of malignancy. Palpation of the liver and retroperitoneal structures at the time of the operation revealed no evidence of metastases from the previously resected carcinoma.

Recovery was uneventful and the patient discharged from the hospital 1 month after operation, after having been fitted with Koenig-Botz bag. Periodic follow-up examination was made post-operative eight months after the second operation. He had regained strength and weight and the ileostomy was being managed satisfactorily.

**Comment**—In this patient it was deemed advisable to resect the transverse colon, the left colon, rectum and anus because of the presence of three malignant nodules, one in the transverse colon, one in the splenic flexure, and one in the rectum. The age of the patient and the preoperative condition after adequate preparation justified doing this procedure in one stage. The development of polyps in the remaining portion of the right colon apparently followed the earlier resection and produced symptoms which required the removal of the remaining portion of the colon and the establishment of an ileostomy.

**CASE 2**—J. R., 40 years old, was admitted to the surgical service of the Jewish Hospital on July 20, 1946, complaining of diarrhea which had been slowly progressing in severity for one year. The symptoms began with episodes of two to three loose stools per day not associated with tenesmus or bleeding. The course was characterized by remissions lasting for one or two weeks but each succeeding attack of diarrhea became more severe and for three weeks before admission the stools had increased to eight or ten per day associated with the passage of mucus and bright red blood, and with tenesmus. There had been a weight loss of fifteen pounds (135 to 120 pounds) in the two months before admission. Her brother (R. K. (Case 3)) had had resection of the colon for polyps at the Illinois Research Hospital six months earlier. There was no other familial history of suggested polyps or carcinoma of the colon. The patient was the mother of three children, aged 6, 12, and 13 years, who were apparently in good health.

**Preoperative Study and Preparation**—On physical examination the patient appeared slightly underweight but otherwise did not appear ill. Upon digital examination of the rectum, multiple small, sessile polypoid protuberances of the mucosa could be felt, beginning at a distance of 4 cm. from the anal edge. There was evidence of ulceration in a polypoid lesion 7.7 cm. on the posterior wall of the rectum. A biopsy of this area revealed adenocarcinoma. Proctoscopic examination for a distance of 34 cm. revealed innumerable areas of sessile nodules and other protuberances which were papillary in structure and pedunculated. The largest mass was in the sigmoid colon, a distance of about 17 cm. and it was pedunculated and cauliflower-like with areas of ulceration. The mass measured about 6 by 2 cm. Biopsy of this area revealed malignant change. Study of the colon with a contrast medium revealed innumerable oval filling defects extending from the ileocolic junction to the rectum (Fig. 2). Laboratory data included the following: the red blood cell count was 4,270,000, the hemoglobin 13 Gm. and the white blood cell count was 4,200. Protopor-



Fig. 2—J. R. Results of barium enema. (a) barium with air contrast media.

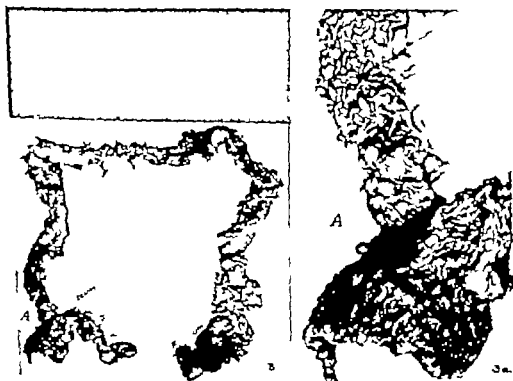


Fig. 3—J. R. Specimen removed in one operation. (a) stage polyp.

(b) Illustration of re. 4 to show



1. preparation consisted of low residue diet and preparation of the bow. 2. ileal and Sulfasalazine

**Surgery.**—On Jan. 26, 1946, through transverse incision extending for both flank total colectomy and abdominoperineal resection of the rectum and anus were performed in one stage with the establishment of an ileostomy.

**Pathology.**—Pathologic examination of the specimen removed at operation (Fig. 3) revealed innumerable polyps, of which some were sessile and others pedunculated, extending from the ileocecal junction to the mucosubcutaneous junction of the rectum and anus. There were no symptoms of the lower sigmoid and in the sigmoid anaplasia, as revealed on proctoscopic examination. There was no extension of polyp formation into the terminal 3 inches of ileum which were removed at operation.

**Postoperative Course.**—The postoperative course satisfactory for period of 31 days. The Miller-Abbott tube which had been inserted before operation was removed on the 13th day. On the fifth day lower abdominal tympanitic evidence of small bowel obstruction developed, and the Miller-Abbott tube was reinserted and removed 4 hours later. The ileostomy had functional satisfaction from the 13th to the fifth day but less the Miller-Abbott tube as removed on the sixth postoperative day symptoms of small bowel obstruction again developed. On the eighth postoperative day exploration was carried out on the patient by reopening the right half of the incision and transverse incision. A tumor of the ileum not felt on it at an angle of 15 degrees was found at the junction of the ileum with the abdominal wall. The distal four inches of ileum were resected and new ileostomy was established. The abdomen was closed through and through sutured incisions. The postoperative course was marked by mild pain and temperature of 100.1 to 101.0 F but there were no signs of peritonitis. The pulse and temperature subsided in period of five days and the convalescence from this point unremarkable. The patient was fitted with Koenig-Rotter bag and was discharged from the hospital on March 2, 1946, five weeks after the initial operation.

**Follow-up.**—Follow-up was carried out on the patient for 12 months. The patient regained full strength and weight as well as free symptoms, and found the Koenig-Rotter bag little burden with the use of the Koenig-Rotter bag. Her three children are subjected to studies of barium enema and colonoscopy. They were found to be free of symptoms and had no objective evidence of pathology but they are being examined at early intervals for the presence of polyps.

**Comments.**—In this patient the cause of colitis was of conjugal violence of malignancy. Change in the polyps, in the rectum and in the colon in the lower sigmoid. The presence of an anomaly in these areas indicated a plan of less radical therapy than that which was done for removal of the colon, cecum and anus. The good health, lack of obesity and no serious illness were all factors favorable for doing the procedure.

**Case 2.**—J. C. White was aged 46 years, married, and the subject of severe (the University of Illinois Hospital on Dec. 1, 1946, a chief complaint of large irregular bowel habit and red blood color of the stool. The patient stated that for four years he had been having these symptoms. Each morning and on occasional occasions he was having severe pain in the lower abdominal movement that he usually had before the onset of the illness. He had noticed blood and mucus in the stool on a number of the past few months. There was no history of weight loss, the patient had remained good, and he had no labor and or anal discomfort. There was no family history of disease of the large intestine.

**Preoperative Study and Preparation.**—On physical examination the patient did not appear to be ill and was making no abnormal findings of importance. Upon digital examination of the rectum firm nodular masses were felt at the top of the finger. Proctoscopic examination revealed a flattened polypoid mass on the posterior wall

right lateral wall of the rectum 1 height 1.8 cm and another smaller one 3 cm higher on the left wall of the rectum posteriorly at the level of the rectosigmoid junction. Each of these lesions was in diameter and is not least 1 cm above the level of the mucosa. From either lesion a small polypoid mass was removed from 0.5 to 1 cm. size on removal but this was by means of force from the lateral area for biopsy were not a lesion of the rectum. The colon was found to be normal and no evidence of the sigmoid rectum, and on done and a colonoscopy was made at the upper end of the sigmoid colon and the left lower quadrant of the colon.

Pathology.—On Jan 1 1966, a colonoscopy was performed through a low left rectal incision. Pathology of the lower colon, and retroperitoneal structures revealed no pathology. Only low in the area of the sigmoid colon were some small polyps with the lesions. There was no evidence of extension through the mucosa. A colonoscopy was made at the upper end of the sigmoid colon and the left lower quadrant of the colon.

Pathology. Pathologic examination of the specimen (Fig 4) revealed the presence of the adenomatous polyps in the area of the sigmoid colon. There were ten polyps ranging from 0.5 to 1 cm in size extending from the upper rectum through the lower sigmoid colon.

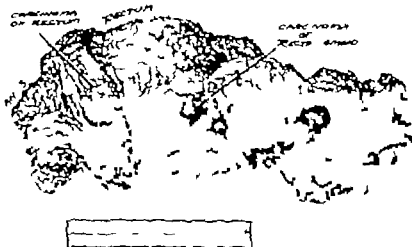


Fig 1-3. Specimens removed. Intraoperative reduction.

Pathology.—The pathology of the specimen was successful and the patient is in good health. The largest polyp was 1.5 cm in size and was found to be adenomatous. The patient was found to have a total of 10 polyps, 5 of which were adenomatous. The remaining 5 polyps were found to be hyperplastic. The patient was found to have a total of 10 polyps, 5 of which were adenomatous. The remaining 5 polyps were found to be hyperplastic.

Comment.—In this patient there was no familial history of polyps and the rectum in all cases appeared to be confined to the distal segment of the left colon and to the rectum. For these reasons this case is not least one of the familial form of polyposis and the development of polyps in the remaining segments of the colon might not occur. Nevertheless, it is planned to study the remaining segment at intervals of 3 to 5 years to see the development of polyps.

CASE 4—R Y white male aged 39 years, admitted to the surgical service of the Cincinnati General Hospital on Aug 21 1947. The chief complaint bloody diarrhea 15 times to twenty stools a day with the passage of much mucus. The onset of the symptoms was on March 22, 1947 6 months before admission. This episode lasted for two weeks and then subsided. Three months later the patient had recurrence of diarrhea lasting three days. He then became markedly constipated, requiring cathartics for bowel movement. Three days before admission diarrhea recurred, with the appearance of copious amount of red blood with the stools. During the 4 months before admission the patient had lost twenty five pounds in weight and had developed weakness and anorexia.

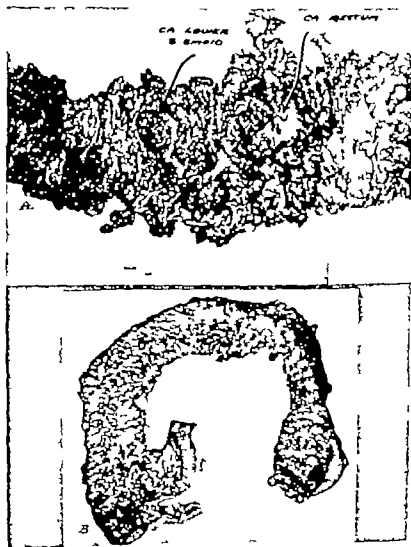


FIG. 8.—R Y A, Specimen removed first operation. B specimen removed second operation.

In the 4 hours before diagnosis she had experienced chilly sensations, had vomited, and become exhausted.

The father of this patient died in the Cincinnati General Hospital on Sept. 14, 1935 at the age of 43 years, here he had been admitted for terminal care for advanced carcinoma of the colon secondary to polypus.

**Preoperative Study and Preparation.**—Physical examination revealed emaciated, slightly cyanotic and pale young woman who appeared markedly undernourished and anorectic. The temperature was 99.6 F the pulse was 110 and the blood pressure was 95 systolic and 50 diastolic. On digital examination of the rectum, closely set multimodular masses were felt which were variable size. A hard, raised, nodular mass as felt on the posterior wall of the rectum at a level of 6 cm from the anal verge.

On sigmoidoscopy examination there were multiple polyps varying in size from 0.2 to 1.0 cm beginning at the junction of the sigmoid with the rectum. At the level of 8 to 6 cm there was a large, rarefied, hemorrhoidal ulcerating mass which appeared neoplastic and which extended upward for a distance of about 4 cm. From this point a distance of the limit of the gross scope (4 cm) the wall was studded with multiple closely set polypoid nodules occasional areas of ulceration. Biopsy of the hemorrhoidal mass revealed adenocarcinoma, grade. Barium enema 18 days after admission showed numerous rounded filling defects which were scattered throughout the entire large bowel.

The general appearance of the patient was one of desperate illness. She was placed on intravenous support regime which included the transfusion of whole blood, the intravenous administration of glucose and amegon, and the parenteral administration of vitamins B, C and K, sulfadiazine and penicillin. She was also given Sulfadiazine by mouth. The diarrhea and fever subsided in about three days but the patient then refused oral feedings because of nausea. The feedings were resorted to for a few days and she then began subsequent oral intake as her regimens from time to time loose stools a day. All the preoperative preparation extended over a period of 2 weeks. By this time she had gained in weight from 4 to 5 pounds and the temperature, pulse and respirations had become normal.

**Operation.**—On September 30, six weeks after admission to the hospital, combined abdominaloperational resection of the rectum and anus was done.

On January 1, 1936, 3½ months after the resection of the rectum the remainder of the colon removed and ileostomy as done. The first operation was done through left paramedian lower rectum incision and the second through wide transverse incision extending from flank to flank. The patient withstood both operative procedures well and healed well.

**Pathology.**—Pathologic examination of the first specimen revealed two areas of carcinoma, one in the rectum measuring 3 cm in diameter and close to the rectosigmoid junction, measuring 1.5 cm in diameter (Fig. 3 A). The resected specimen contained numerous low-set polypoid nodules some were sessile and others filiform. At the resection of the sigmoid, the masses were studded with numerous polyps. Pathologic examination of the right transverse and descending colon showed disseminated polypoid nodules that found the other segment (Fig. 3 B). There were no further areas of carcinoma.

**Postoperative Course.**—The postoperative course after the stage of surgery was uneventful.

**Comment.**—If this patient had been seen a number of years ago before the advent of modern supportive therapy and chemotherapy a preliminary ileostomy would have been required to put the colon at rest and overcome colitis due to secondary bacterial invaders. She was so ill that the load superimposed in the ileostomy might have resulted in death and certainly would have entailed additional risk. The long interval was allowed between abdominaloperational resection and the later colectomy in order that the patient might gain in weight and

strength. Because no real intestinal obstruction had been suspected from barium enema with air contrast media above the level of the rectosigmoid, the delta seemed justified. One month after the second operation the patient was fitted with a Koenig Rutzon bag and was discharged from the hospital. She is now in good health and free of symptoms.

#### CASE 5—

**History.**—R. K., 41-year-old male, first admitted to the Margulies Service at the Research Hospital, New York, on March 2, 1944. The patient's chief complaint was of intermittent diarrhea with occasional bloody stools which had been increasing in severity for periods of 3 to 5 years. The preceding 3 to 4 months the diarrhea and symptoms had increased to the point where he was passing continual bloody stools. Weight loss had been 50 lbs. possibly and the patient was 160 lbs. and 5 ft. 10 in.

**Proctoscopic study.**—The colon showed diffuse polyps with an ulcerating lesion in the posterior rectal wall. Fluoroscopic and double contrast studies showed diffuse polyps of the entire colon except the cecum. The ulcerating lesion on the posterior rectal wall, 3 cm. above the peritoneal line, measured 1 cm. in diameter and biopsy showed adenocarcinoma, grade 2. At the time of this admission, no family history of carcinoma or polyps of the colon could be obtained from the patient.

**Surgery.**—On March 13, 1944, an extensive combined intraabdominal resection of the lower sigmoid, rectosigmoid and rectum was done in the manner of the Mile procedure. At operation, there was no evidence of lymph node metastasis in the mesosigmoid or retroperitoneum and the liver was grossly free of evidence of metastatic disease. The remaining colon, which was not removed at this time, showed 1 cm. pieces of diffuse polyps, there being present small polypoid nodules throughout the entire colon to the cecum. A left single lacerated colostomy was exteriorized through left iliac wound incision. The patient's postoperative course was excellent. He was observed for one year and that time no evidence of recurrence was present. One year later, however, the patient was readmitted to the Research Hospital, and on March 19, 1945, a second colostomy was done removing the rest of the colon, round to the cecum. At surgery there was evidence of recurrent cancer in the bladder. The cecum was exteriorized through right wound in the right lower rectal muscle. The patient's postoperative convalescence was unremarkable.

**Pathology.**—The first specimen resected in March, 1944, showed carcinomas of the rectum on the posterior wall which had not penetrated through the muscle layer. The lesion measured 4 by 4½ cm. in diameter and macroscopically showed grade adenocarcinoma. Lymph nodes examined were negative for evidence of metastatic disease. The rest of the specimen showed diffuse polyps with 1 grade 2 adenocarcinoma. The second specimen resected one year later of the remaining portion of the colon around to the cecum, showed diffuse polyps, the masses being typical of 1 to 5 mm. in diameter. The adenocarcinoma was examined macroscopically showed atypical karyotype but were interpreted as being distinctly precancerous.

**Follow-up Study.**—The patient was examined at regular intervals after the first operation and showed no evidence of recurrent cancer. He required eight physical examinations and blood counts were normal and he has been working but not full-time since.

**Comment.**—This patient is the brother of J. R. (Case 4) who was operated upon almost 15 years later by one of us (J. I. H.) in Connecticut. Occurrence of disease in this patient's brother was the first evidence of a familial tendency in this particular patient. In this man, cecostomy was done rather than a colectomy for three reasons. First, the cecum was not involved with polyp formation; second, it was desired to preserve as far as possible the debulking function of the cecum; third it was felt that further recurrence of polyps could

be reached by regular examination of this small segment through a proctoscope until it into the rectum, and the fulguration of polyps as they appeared could be easily performed. To date no polyps have occurred in this remaining segment of rectum.

#### CASE 6—

**History.**—A married white woman, 30 years of age, was first examined in the early third decade at the Loomis and Educational Hospital in Chicago, March 20, 1947. Chief complaint at that time was bloody stools daily for the preceding 2 years. Proctoscopic and roentgenologic examinations of the colon at that time showed evidence of diffuse polypoid of the colon with mucosal hypertrophy of the rectum, rectosigmoid, and right colon. Maximal anal opening was 1½ inches, decreased by anal transverse colon. Diagnosis of diffuse polypoid of the colon. On three occasions the patient was admitted to the hospital for proctoscopic fulguration of the polyps. She became pregnant, and no further treatment was given during pregnancy. In October 1948 the patient gave birth to a male child. Following the delivery she experienced increasingly frequent cramping pain in the abdomen. This gradually progressed and patient developed bloody diarrhea of ten to fifteen stools daily. She lost 25 lb. in the course of 6 months. The patient became weak from blood loss and eight days before giving birth to the hospital in March, 1949, for delivery and treatment for the polypoid of the colon.

**Physical Examination and Preparation.**—Physical examination revealed pale and thin but not emaciated, undernourished and underweight. She was not acutely ill, and temperature, respiratory rate, and pulse were normal. The pulse 90 beats per minute, rather marked normal sinus rhythm. No murmurs were noted on general physical examination. Red blood count 10,000 hemoglobin 10 gms and the patient was hemoglobin 10 gms. General blood work showed the patient placed on low residue high protein diet. A suppository was given at the time of the physical examination. On March 1, 1949, all polyps of the rectum and rectosigmoid of a distal 10 cm. were removed by fulguration through the operating proctoscope. There were only three polyps which were in clusters destroyed. These polyps were small, pale and scattered and it was possible to obliterate them completely.

**Surgery.**—On March 4, 1949, laparotomy performed under spinal anesthesia through lower midline incision. Exploration revealed diffuse polypoid involving part of all the upper sigmoid and descending and transverse colons around part of the cecum flexure and the ascending colon. The gross tumor transected four inches from the peritoneal reflection, and the rectosigmoid removed. The anal opening closed. The blood supply of the cecum (the main mesocolon) was cut and the cecum was swung around the pelvis and anastomosed to the rectosigmoid by an end-to-end anastomosis, using two-ligature technique. The incised colonic in the external wound was sutured. The patient made an unremarkable recovery and discharged from the hospital fifteen days later.

**Pathology.**—The mucosal specimens of the colon showed diffuse multiple polypoid throughout the mucosal specimens. The distal end had no polyps and there were none in the far end and one half inch above the resected line showing that the resection was below the level of the previous fulguration through the proctoscope. The polyps faded out in the ascending colon and there were none within one inch of the level of transection through the colon. The polyps were all benign, and none showed malignant changes, nor were there any evidence of invasion.

**Follow-up and.**—The patient regained her normal weight and at the time of this report had three soft formed stools daily without any loss of blood. She showed normal bowel function and felt entirely well. Frequent proctoscopic examination showed recurrence of one polyp one year later in the anal rectosigmoid. This was destroyed by fulguration. Since then, no other polyps occurred. The anastomotic enteric line was normal, and small portions of the remaining colon can be examined. There are no evidence of polypoid here so far.

**Comment.**—There is no familial history so far of polyposis in this patient's family. She has improved remarkably since the area in the colon containing the polypoid mass was removed. It is believed that it is a safe procedure to do an end-to-end anastomosis of this type since the remaining colon can be visualized proctoscopically and more completely roentgenologically at frequent intervals. Preservation of the cecum here was done again to preserve the dehydrating function. The surgeon felt that in this case an ileosigmoidostomy would have produced a diarrhea which would have been less of a relief than was a sigmoidostomy.

#### CASE 7—

**History.**—A 68-year-old male aged 64 years, admitted to the Presbyterian Hospital in Chicago, in January 1933. On Jan. 17, 1923, exploratory laparotomy and left sigmoid colectomy in preparation for resection of carcinoma of the rectum were done. On Jan. 21, 1931, several benign polyps were removed from the colonoscopy stoma. On Feb. 2, 1933, posterior resection for carcinoma of the rectum was performed. In 1929 the patient developed obstruction, and carcinoma of the spleen, the surface of the colon was found and removed by the obstructive resection procedure. This colectomy was later closed and the lower sigmoid colectomy remained. The functioning colonoscopy stoma. The patient was hospitalized on several occasions in 1944 for drainage of abscesses around the stoma. In April 1945, transurethral resection of the prostate was performed. Shortly afterwards it became apparent that another cancer was present in along the colonoscopy stoma with extensive involvement of the skin and muscle about it. The patient as a very advanced condition from the natural suppuration and discharge about the colonoscopy and the recurrent cancer involving the abdominal wall about it. There is signs of beginning obstruction at this point.

**Present Preparation.**—Physical examination revealed an elderly, poorly nourished, but male 64 years of age, who was relatively ill. The daily temperature chart showed range up to 101 and 102° F. daily. The pulse was around 95. Red blood count was 4,000,000 and hemoglobin 9 Gm. Physical examination showed extreme swelling of the abdominal wall, back, scapular and along the evidence of marked right loss. The left lower quadrant of the abdomen involved with nodular gray recurrent tumor. Multiple draining sinuses from abscesses about the colonoscopy stoma. Biopsy of the tumor about the colonoscopy showed adenocarcinoma, grade 3. The patient as placed on low residue high protein diet and supplementary parenteral feedings of milk serum.

operation through an incision in the midline just medial to the line of the colonoscopy. In exploring the abdomen, two other carcinomas of the right transverse colon were found, but no involvement of the liver was apparent. There were multiple small metastases. The transverse mesocolon. Further exploration revealed that the extension of carcinoma about the colonoscopy potentially resectable. The distal loop leading from the double-barreled left sigmoid colectomy down to the peritoneal floor, here the original posterior resection incision was markedly distended because of obstruction of the colonoscopy. Several sinuses. This practically constituted a local loop obstruction. The bowel was markedly thickened and there was marked scarring in the pelvic area. The distal loop was freed from its pelvic thickening through a rather difficult sharp dissection, and brought out of the abdomen. The entire colonoscopy area was the removed by sharp dissection, removing full thickness of the abdominal wall in a rather wide area. A subtotal colectomy was then performed in one stage round to the cecum. Nothing could be felt in the cecum, and since its blood supply appeared to be adequate, the colon

was removed, this point and the cecum exteriorized through a stab wound in the right lower rectus muscle. At the time of this procedure the only evidence of metastatic disease as in the lymph nodes of the transverse mesocolon, and as far as could be determined, these were removed completely. Closure of the abdominal wall was very difficult because a large portion of the left lower quadrant had been removed. It was through and through single layer closure, however, a perfect under marked tension. The patient's postoperative course otherwise as stormy but better than had been anticipated. Antibiotics parenterally and continuous intestinal decompression provided the margin that probably allowed for recovery. The wound healed slowly and by sexual infection, and one ulcerating area required a grafting of a later date which was four weeks later removed 3 weeks after the laparotomy.

**Pathology.**—The specimen showed carcinoma arising in the left lower sigmoid colon, growing and extending widely into the surrounding colon, all three. As far as could be ascertained, the extension was removed completely. There was a second carcinoma in the distal segment below the peritoneum, which had not been recognized at surgery because of the thickening of the colon in this distal loop. The two carcinomas in the right transverse colon which had been observed at surgery showed typical fungating and ulcerated polypoid growths, adenocarcinomatous. There was a third carcinoma at the hepatic flexure which had not been recognized at surgery. This was a rather small lesion measuring 3 cm. in diameter, but as definitely malignant. The rest of the specimen showed many pedunculated polyps averaging up to 1 cm. in diameter. Examination of many of the polyps showed three of them to have definite carcinomatous changes, which were not recognized grossly. The polyps showed varying degrees of dysplasia.

**Follow-up History.**—The patient survived the operation, gained weight and felt quite all for six months. A recurrent tumor developed in the right lower abdomen, medial to the cecum, in the fall of 1943. This was fixed and hard. It was obviously recurrent cancer. The patient course rapidly downhill, and he died Nov. 10, 1943.

**Copy of Material.**—Autopsy examination of the body showed multiple liver metastases which were the ultimate cause of death, in multiple intraperitoneal and retroperitoneal nodes arising from desmoplasia.

**Comment.**—This case is an example of multiple polyposis which demonstrates the extreme tendency of this disease to produce carcinoma of the colon. Over a period of fifteen years this patient had at least eleven separate adenocarcinomas of the colon which obviously arose on the background of the pre-existing diffuse polyposis. We were unable to obtain from his family any history of a familial tendency, and there are no siblings or other relatives so far who have developed polyps or cancer of the bowel.

#### FINAL ANALYSIS OF CASES

These seven case reports, added to the preceding summaries, make a total of thirty-five cases of polyposis (reported in the American literature since 1930) in which attempt at surgical cure had progressed to the point of removal of portions of the large bowel (Tables I and II). In examination of the summaries, considerable variability is noted in the chronologic order of the surgical procedures used to accomplish end results. In some cases the variations were necessary because of manifestations of the disease peculiar to the individual. In others they were caused by failure of the first operator to appreciate the disseminating and premalignant qualities of the disease, attention at first being directed to segmental resection. In all cases the only two methods resulting in cure were total ablation of the large bowel and external ileostomy, or total colecte-



TABLE I. SURVIVAL WITH FULGERATION

CASE NO.	PROCEDURE	CHRONOLOGY OF STAGES	A. NUMBER OF STAGES	INTERVAL BETWEEN STAGES	LOCATION OF CAR CT. CYCLES	RESULT (Y. TIME OF REPORT)
1	Heur-tom; colectomy fulguration, ileocecectomy		4	10 mo	None	Living 8 yr
2	Heur-tom; fulguration, colectomy (Rachin)		3 mo	4 mo	None	Death from peritonitis and pulmonary embolism attributed to a severe episode of sigmoid stricture due to polyps
3	Fulguration, right colectomy and ileocecectomy; left colectomy fulguration from bare closure of sigmoid colectomy		6	Not stated	None	Living 6 mo
4	Fulguration, right colectomy and ileocecectomy (Mayo and Gelfand)		3 mo	Not stated	None	Death days after laparotomy for intestinal obstruction after stage 2
5	Fulguration, colectomy and ileocecectomy (Jones)			4 yr	None	Death from carcinoma 10 years later
6	Fulguration, colectomy and ileocecectomy (Hickman)		2	3 mo	None	Living 12 yr
7	Fulguration, colectomy and ileocecectomy; fulguration recur rent polyps (Lahry)		3	Not stated	None	Living 10 yr
8	Fulguration, ileocecectomy and left colectomy; fulguration, removal of rectum		4	4 yr	None	Living 3 yr
9	Fulguration laparotomy and anastomosis (pull-in reaction)			1 yr	Rectum	Death 4 days after reaction
10	Fulguration, ileocecectomy and colectomy (Pfeiffer and Patterson)		3	6 mo	None	Living 1 yr
11	Fulguration, ileocecectomy; colectomy (Pugh and Newell)		1	3 mo	None	Recovered
12	Fulguration, ileocecectomy; right colectomy; left colectomy fulguration through sigmoid; ileocecectomy; ileocecectomy; resection of sigmoid and ileocecectomy for carcinoma; resection of rectum for carcinoma		5	8 yr	Rectum	Death from rectal carcinoma 1 yr later
13	Fulguration, ileocecectomy; right colectomy; left colectomy; resection of sigmoid, and ileocecectomy (O'Neil)		3	11 mo	None	Living 1 yr
14	Fulguration, colectomy and ileocecectomy; resection of sigmoid (Hicks and McHugh)			2	None	Living 2 yr
15	Resection of sigmoid, fulguration ileocecectomy and colectomy (Pfeiffer and Patterson)		4	18 mo	Sigmoid & rectum	Survivor of carcinoma on rectal carcinoma 10 mo
16	Transverse colectomy; resection of sigmoid, fulguration, colectomy and ileocecectomy		4	7 mo	Midgut small	Living 5 1/2 yr
17	Fulguration, transabdominal resection of polyps, fulguration, total colectomy and ileocecectomy (Gardner)		4	4 yr	Colon	Living 10 mo

TABLE II. SUMMARY WITH OCT FOLLOW-UP

CASE	1. NATURE AND CHRONOLOGY OF STAGES	NUMBER OF A.D.	INTERVAL BETWEEN A.D.	LOCATION OF CANCER	RESULTS (AT TIME OF REPORT)
15	Neostomy colectomy rectal resection	3	7½ mo	Rectum	Death 11 mo.
19	Neostomy colectomy rectal resection	3	3½ mo	Rectum	Living 3 y
20	Neostomy colectomy rectal resection	3	6 mo.	None	Recovered
21	Neostomy colectomy rectal resection (1½ hr)	3	3 mo	None	Living 1 y
—	Neostomy rectal resection, colectomy (Hearshorn)	3	6 mo.	Rectum	Living 3 y
23	Neostomy colectomy rectal resection (Hugh and Needell)	3	5 mo	None	Recovered
4	Rectal resection, colectomy (Lalor)	(1)	1	(4) sigmoid, rectum & colon	?
5	Right colectomy left colectomy rectal resection (W. Leaky)	3	3 mo	None	Recovered
26	Rectal resection, colectomy		3 mo	Rectum	Living 3 y
27	Rectal resection, colectomy (M. Her and Sweet)		1 mo	Colon, sigmoid, rectum (3)	Living 7 y
28	Rectal resection colectomy (O. P. Hall)		4½	Rectum & sigmoid (3)	Cancer of blood anal all time of colectomy
29	Sigmoid colectomy rectal resection, resection of pleural flexure colectomy & resection	4	1 yr	Colon, sigmoid, rectum (6)	Death 6 mo from metastatic carcinoma
30	Resection from cecum left colon & rectum, right colectomy		4 yr	Transverse sigmoid rectum (3)	Living 1 yr
31	Rectal resection, colectomy deferred	(1)	1	Rectum sigmoid, rectum (1)	Living 1 y
32	Rectal resection, colectomy		½ mo	Rectum sigmoid rectum (1)	Living 1 mo
33	Rectal resection colectomy & resection		1 yr	Rectum	Living 1 y
34	Resection of colon from cecum, sigmoid (Holworth and Haughton)	1	None	Rectum	Living 1 yr
35	Colostomy right and colectomy resection resection of sigmoid with thickened sigmoid & sigmoidal colon closure of colostomy stoma	4	3 mo	(1) Cecum & sigmoid	Living 1 mo

TABLE III

LETTER	TIME	TIME	AGE	TIME	OF	APPROXIMATE PERCENTAGE
1	Presence of carcinoma in rectum or sigmoid			1	Absence of carcinoma in rectum or sigmoid	
—	Closest net polypoid tissue and carcinoma				More sparse distribution of polyps in lower segment	
3	Imprisoned in prolonged follow-up			1	Complete patient and families for prolonged follow-up	

tomy and ileosigmoidostomy (or ileoproctostomy) combined with fulguration of the lower segment (Fig 6). A review of the experiences encountered in these thirty five cases should aid in the establishment of a more lucid concept of the surgical treatment of polyps.

It will become apparent as the discussion progresses that no attempt should be made to hold one method of treatment in favor of the other except as applied to the individual patient. The method which preserves sphincter function is to be preferred provided rigid conditions for its safety are established. Otherwise it probably should be discarded in favor of the other plan.

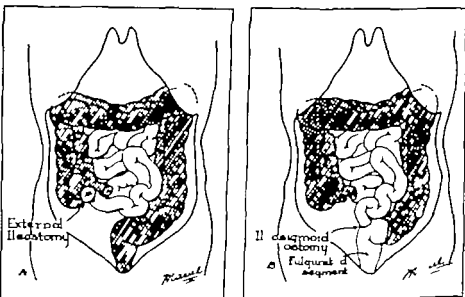


Fig 6—Diagrams showing end stages of the two methods of treatment. A Total ablation B colectomy with ileosigmoid anastomosis

Total removal of the large bowel is the method of choice if there is indisputable or even questionable evidence of carcinoma of the rectum or low sigmoid colon. Even those who favor preservation of the sphincter mechanism in patients with cancer of the rectum probably would not care to preclude ileoproctostomy by fulguration of polyps in close proximity to the cancer. Total removal might also be preferred if the rectum exhibits closely set polyps with marked hyperplasia, ulceration, and secondary infection. Under these conditions areas selected for biopsy may not be representative and carcinoma can be overlooked (Table III).

Total ablation may be done in one or multiple stages depending upon the health, age, sex, and obesity of the patient, and his course during surgery. One case in which these conditions were so stable for operation in one stage has been presented (Case 34). The summary of these cases indicates that if cancer of

the rectum is present and stage operations are employed, resection of the lower segment by combined abdominoperineal approach should be done as the first stage without preliminary ileostomy if the patient can be adequately prepared and there are no signs of obstruction. At this stage resection should be carried proximal to the point of other carcinomas suspected by roentgenologic evidence or found on laparotomy (Case 30). Colectomy and ileostomy may then be done as a second stage. Results obtained by use of this method have been excellent (Cases 26, 27, 29, 30, 33, and 34).

The review indicates that use of preliminary external ileostomy in patients known to have carcinoma of the sigmoid or rectum is generally undesirable because of the long interval imposed by waiting for systemic adjustment or by management of local complications of the ileostomy before curative resection can be done. In six instances in which ileostomy preceded rectal resection the average interval between the two procedures was 6 months, 3½ months being the shortest and 9 months the longest (Cases 18 to 23). In three of these cases cancer of the rectum was identified before ileostomy was performed (Cases 18, 19, and 22).

The object in producing an ileostomy is to effect improvement in the general health of the patient and in the local condition of the bowel (in order to facilitate handling) by defunctionalizing the colon. For a considerable period of time improvement in health is delayed because of the additional burden placed upon the patient by the abnormal loss of essential elements of nutrition until adjustment is made. Admittedly this is still a necessary imposition in the surgical management of many cases of diseases of the colon which are primarily inflammatory. Secondary inflammation in polyposis of the colon probably can now be controlled satisfactorily in most instances by the use of oral feedings of suitable content combined with an intelligent use of chemotherapeutic intestinal intubation, whole blood and other forms of parenteral feeding. In their application of these measures in resecting the scope of surgery that can be performed in one stage and result in fewer stages and contracted intervals of treatment.

While long intervals of delay between rectosigmoid resection and completion of the ileostomy are not desirable (Cases 25 and 29) not a much risk is entailed as when there is delay in resecting the lower segment. This is apparent upon scrutiny of the incidence and location of cancer in the tabulated cases (cancer was present in the rectum, rectosigmoid, or sigmoid in seventeen of the thirty-eight patients (see Tables I and II). In seven cancer was identified proximal to the rectosigmoid area, and these were accompanied by cancer of the lower segment in four instances (Cases 4, 27, 29, and 30). In three patients cancer was present in the proximal areas without involvement of the lower segment (Cases 16, 17, and 3).

The method which combines fulguration with surgery was employed with considerable success in sixteen of the thirty-eight summarized cases. Analysis of the reports make point to the factors which influence its success or failure and aid in establishing its limitations. Obvious preference should not be given this method in any patient unless the possibility of cancer in the rectum or

lower sigmoid is eliminated after a careful search. The presence of cancer here in seventeen of the thirty-five cases indicates the close observation which must be accorded this segment if it is allowed to remain.

In some of the seventeen patients treated by this method, death resulted from cancer of the rectum in from one to six years after fulguration was begun (Cases 9, 12, and 13). In one of these (Case 5) fulguration was repeated over a four-year period after which colectomy and ileosigmoidostomy were done; the patient died two years later of carcinomatous metastases. In another (Case 9) fulguration preceded laparotomy by one year and a palliative resection was done. In the two others there were intervals of  $5\frac{1}{2}$  years and 1 month between fulguration and colectomy with ileosigmoidostomy (Cases 1 and 11).

Failures which result from the use of this method are not necessarily indictments of it since they can be attributed to various other factors. Certain criticism of the method, if it has been applied honestly, appears to be justified after a careful examination of the case report.

Definitely increased fulguration rather than the low sigmoid and rectum, the presence of cancer should be excluded by careful study of the gross morphology of the mucosa, well below the rectosigmoid region and of the microscopic anatomy of sections obtained from representative areas. Early carcinoma in situ may be difficult to recognize.

The presence of loosely set polyps increases the difficulty of interpretation and markedly prolongs the interval required for cancer destruction and healing. Persistent attempts to follow the programs of fulguration when polyps are closely set may result in perforation or leakage of the sigmoid stump after closure (Cases 9 and 19). Interruption of the treatment in some instances are due to unwillingness of the patient to submit to a large number of antineoplastic procedures, especially to repeated removals, resulting in a symptomatic improvement.

Ten of the seventeen patients with intestinal neoplasms were reported as living and without evidence of recurrence of carcinoma from six months to twelve years after operation (Cases 1, 3, 6, 8, 10, 13, 14, 16, and 17). Interval between fulguration and colectomy in these cases varied from three months to the shortest interval necessary for the best effect. In the future to reduce the interval of time between fulguration and colectomy should result in a greater percentage of cures. Once the rectum is freed of polyps and ileal neostomies are made repeated examination of the low segment of the bowel and fulguration of recurrent polyps is imperative.

Because of the differences in the radiation of this use, the small number of cases in each series, and the short period of follow-up, no attempt should be made to state a result obtained in this use of the accepted methods for treatment of polyps.

#### SUMMARY

The features distinguishing polyps of the colon as a disease entity are its tendency to occur in certain segments, the diffuse involvement of the colon

with polyps, and the persistence of the lesion early and rapid malignant change. It can be differentiated from the more frequent occurrence of isolated polyps, cancer and inflammatory diseases of the colon and rectum by a careful history, stool examinations, sigmoidoscopy and roentgenologic study after barium and air enemas.

Cure of polyposis depends upon its recognition as a disease entity and its differentiation from other diseases before surgical management is planned. Failure to do this may result in inadequate treatment. Surgery should be directed toward either total ablation of the large bowel or total colectomy and ileocolic (ileorectal) anastomosis combined with fulguration of polyps in the preserved segment.

An analysis of the thirty-five cases presented in which operation was done points to factors to be considered in both the choice of the method to be used and the chronology of the stages employed.

Early recognition of the disease and the increased amount of surgery that can be performed in one stage because of modern therapeutic advances in intestinal surgery combine to give an improved prognosis in polyposis of the colon.

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# RESECTION OF RECTUM AND RECTOSIGMOID WITH PRESERVATION OF THE SPHINCTER FOR BENIGN SPASTIC ILEOIONS PRODUCING MEGACOLON

## AN EXPERIMENTAL STUDY

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TWENTY patients with a clinical diagnosis of Hirschsprung's disease or congenital megacolon, have been studied at The Children's Hospital in the course of the past two years. By the use of special roentgenologic technique it was possible to demonstrate in all of these patients, an area of spasm in the rectosigmoid or rectum at the lower limit of the area of dilatation of the colon (Fig. 1). The technique used consisted of the slow instillation of a barium enema under fluoroscopic observation until the lowest portion of dilated bowel was seen. The flow of barium was then stopped and the bowel was manipulated through the abdominal wall with the patient under the fluoroscope. The area of spasm could then be demonstrated without being obscured by the contrast-filled and dilated sigmoid (Fig. 2).

The disease was characterized in all the children by severe constipation, with bouts of obstipation, dating back to early infancy and tending to become more severe and distressing as the children grew older. Malnutrition in varying degree was present. The length of bowel involved and the degree of spasm probably account for the variations in the severity of the disease.

In the mild case treatment with a regime of Mechoyl, mineral oil, and enemas, as suggested by Low, has been successful. In the more severe cases the use of Mechoyl has caused violent cramp-producing peristalsis, often visible through the abdominal wall. This hyperactive peristalsis has been insufficient to propel the fecal stream through the area of spasm in the bowel in some of the patients. In six of the patients, colostomies above the area of spasm were life-saving measures and completely alleviated the symptoms. In three of these last patients, closure of the colostomy was attempted. In each of the three cases the closure was followed by recurrence of obstruction, and full relief was obtained only by re-establishing a colostomy.

In the severe form of the disease we felt that resection of the spastic area of bowel with re-establishment of bowel continuity would offer a satisfactory means of treatment. However total excision of the area of spasm may require removal of bowel down as far as the anus because the pathological bowel frequently extends to this point. The conventional abdominoperineal resection with permanent destruction of the anal sphincter has obvious disadvantages in the treatment of this benign lesion in child. A method of resection which

permitted removal of the rectosigmoid and rectum, with preservation of the anal sphincter was conceived and is described herewith.

Historically removal of the rectum with preservation of the anal sphincter function has been claimed by the proponent of various operations. Among the first of these was Kraske, who in 1885 advocated an approach posterior to the anus. Removal of the cecum made possible resection of the rectum and end-to-end anastomosis of the bowel. A similar perineal approach was described by Hohenegg<sup>2</sup> in 1889. In executing the second part of this operation the sigmoid was simply pulled through the intact anus and was left protruding without being sutured. An abdominoperineal technique was used by Maunell in 1894 and Weir in 1901 with the added steps of (1) inverting the lower remaining



Fig. 1.—How to position of patient with rectosigmoid as seen after injection of small amount of contrast media into rectum.  
1. 2.—For greater mass of patient the condition similar to that shown in Fig. 1 is which the rectosigmoid can be filled with contrast media obscuring the area of space of



segment of bow 1 and pulling the proximal segment out through this, and of ( ) anastomosing the two ends of bowel with one layer of interrupted sutures. This was essentially the same plan that we had evolved, with the difference that we proposed to extend the resection down to the sphincter and to make an aseptic anastomosis with two layers of fine interrupted sutures in the hope of minimizing the development of stricture.

No experimental work had been done in regard to the latter type of procedure. Therefore it was felt advisable to try this operation on a series of dogs to determine (1) if leakage and sepsis at the suture line would be a problem ( ) if sphincter control could be maintained and (3) if strictures would develop at the line of anastomosis.



## EXPERIMENTAL WORK

Fifteen dogs were operated upon by the technique described here. All dogs used were healthy female adults, of varying sizes. Preoperative preparation consisted of withholding food and fluids for twelve hours. No attempt was made to cleanse the lower intestinal tract. Intravenous nembutal was used as the anesthetic agent. Strict asepsis was observed throughout the operation and no hemostatic or parenteral fluids were used before, during, or after operation.

The abdomen and perineum were shaved and prepared with Zephiran and alcohol and a midline abdominal incision was made extending from the symphysis to the mid-abdomen.

The bladder was retracted toward the symphysis, as was the uterus. The sigmoid was brought into the field and the pelvic peritoneum divided at its reflection from the rectosigmoid (Fig. 3, 1). The rectosigmoid and rectum were freed completely from all attachment in the pelvis down to the anal sphincter.

The bowel was divided between clamps with a carbolic knife as low in the pelvis as possible and the two ends were turned in using two layers of fine silk sutures (Fig. 3, 2). The end of the silk was left long and tied together so that the two ends of bowel were attached by three pieces of silk, each 10 cm. in length (Fig. 3, 3). The abdominal incision was closed in layers, using interrupted silk.

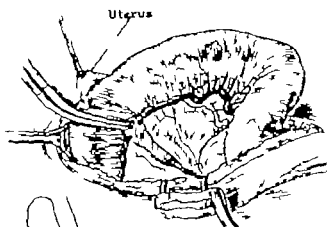
The dog was then placed in the lithotomy position and an Allis forceps, inserted through the anus, was used to grasp the rectal pouch and pull it out into view through the anus (Figs. 3, 4, 5). The whole perineal field, including the everted mucosa of the rectal pouch, was next cleaned, using alternating sponges of Zephiran and alcohol (Fig. 4, 6) and drapes were applied.

With the rectal pouch everted and so greatly prepared, an incision was made  $1\frac{1}{2}$  cm. from the anal skin in a transverse direction through the rectal wall (Fig. 4, 7). This incision gave access to the pelvic cavity and through it the silk suture to the proximal segment of bowel could be reached and the end of this segment pulled down into view (Fig. 4, 8). The proximal and distal bowel were then in approximation with the upper segment telescoped into the lower segment like a finger in a glove (Fig. 4, 9).

A suture line of interrupted black silk was then started between the muscular coat of the everted rectum and the muscular coat of the upper bowel. The lower pouch was cut off as the sutures were placed (Fig. 4, 10). Completion of this suture line sealed off the pelvic cavity from future contamination from the operative site. The proximal bowel segment was opened and sponge soaked in aqueous Zephiran was inserted into its lumen to prevent the flow of bowel contents into the operative field (Fig. 5, 11, 12).

The mucosa was approximated with interrupted 0000 chromic catgut sutures, which were placed as the silk sutures were cut (Fig. 5, 13, 14). After the mucosal sutures were tied and cut the Zephiran pack was removed and the protruding bowel and its suture line replaced through the anus into the pelvis (Fig. 5, 15).

1



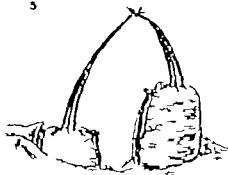
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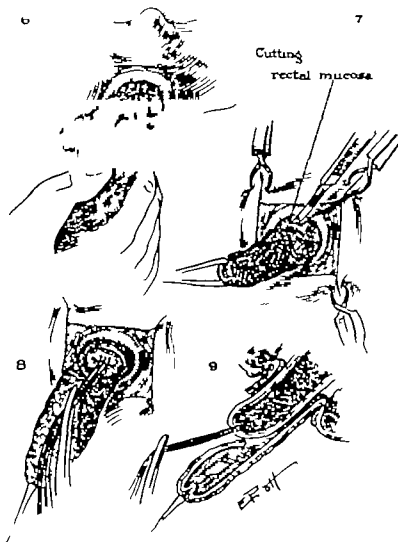
Fig. 1.—The rectum.

Fig. 2.—The rectum and sigmoid colon. The first view shows the rectum and sigmoid colon from a side perspective. The second view shows a more detailed view of the sigmoid colon and its connection to the rectum.

Fig. 3.—The cross-sectional view of the rectum.

Table I shows the results

It will be seen that of the fifteen dogs operated upon, twelve lived and had normal bowel control. Nine were sacrificed on an average of fifteen weeks post-operatively and in each case the anastomosis was found to be well healed without stricture (Fig. 6). Three animals are still living and well. Two of the animals



did not recover from anesthesia after the operation had been satisfactorily completed. One animal died of sepsis and peritonitis, with a breakdown of the anastomosis, three weeks postoperatively.

We felt that our results were encouraging especially in view of the fact that no preoperative preparation of the bowel was done and no chemotherapy

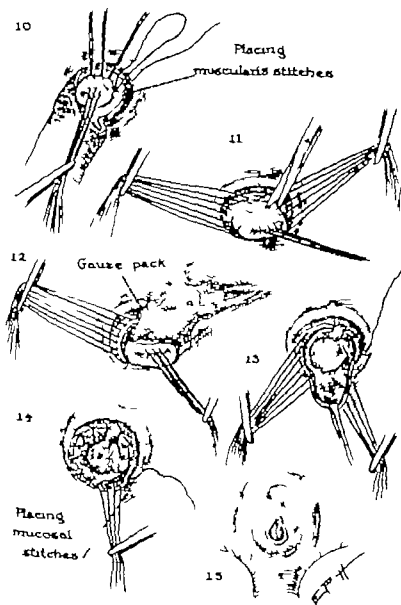


Fig. 5.— Interrupted silk suture is placed through the mucosa, inside of the muscularis. To spread is made by the proximal segment of bow. A gauze pack is inserted to prevent from coming out. The silk suture is cut. The anastomosis is approximated by later placed. The anastomosis is then pushed back through the bow.

used. We were impressed by the fact that the dogs had normal postoperative bowel control and habits, beginning in the immediate postoperative days, and that no stricture developed in any of the nine animals sacrificed (Fig. 6).



Fig. 6.—Photograph of the abdominal cavity in a dog three months after separation. The line of the previous incision indicated by the white cross shows no stricture or infection.

On the basis of our experimental work, the method described was tried on one child. His history follows:

#### CASE REPORT

J. M., boy 6 yrs, 8 months of age, bilateral intercostal emphysema and old picture of paralytic ileus since birth. He was admitted seven times to The Children's Hospital for this disorder starting at the age of 14 months, when he first completely abstained by suspension of feces in megacolon. Conservative treatment gave short relief, but a megacolon developed again after the retrocolic and rectosigmoidectomy described in the previous case. The spastic condition from the low sigmoidectomy did not change.

At the age of 4 years, a new bout of ileus developed sigmoidectomy. The sigmoidectomy was done as described and was followed by removal of the abdominal spinal anesthesia, lumbosacral sympathectomy, and digital rectal examination. The relief of the symptoms was complete. The relief of the symptoms was complete.

Full recovery at the age of 6 years, months, and a child was born of syphilis, during the first year of life. The laboratory. The patient was admitted to the operation performed in the transverse colon was still functioning. The most of bowel to be removed let run and the fact that the bowel does not have sigmoidectomy was known to function normally. Therefore, resection was planned to end from the site of sigmoidectomy to the colon. The area of attachment of the sigmoid colon was the site of sigmoidectomy and the bowel below. The sigmoid colon was removed. The superior hemitransverse colon was divided. The promontory of the uterus and the middle hemitransverse colon were also cut. The lower third of the sigmoid colon was removed. The ends were joined with two layers of silk. The patient

TABLE I. RESULTS OF EXTERNAL HEMORRHOIDS OF RECTUM AND RECTOSIGMOID WITH EXTERNAL ANASTOMOSES PRESERVATION OF THE RECTUM IN FURTHER DOGS

DOG NO. SEX AGE	LIVEST OF LIFE OPER TIME	O 2 W HEALTH	COMMENTS OF AN TUMORS	COMMENTS	
1	Died on 1 hr 2 mo	Unaffected	Excellent	Operation satisfactory animal recovered from anesthesia	normal bowel control
2	2 mo	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
3	8 hr	Unaffected	Excellent	Operation satisfactory animal as if trained in procedure and never recovered from anesthesia	normal bowel control
4	1/2 mo	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
5	10 mo	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
6	10 wks	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
7	10 wks	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
8	10 wks	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
9	4 mo	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
10	10 wks	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
11	8 mo	Unaffected	Excellent	Dog in good health with normal bowel control	normal bowel control
12	3 wks	Infected	Debilitated	Infection (abscess) all of break down of an abscess	normal bowel control
13	6 wks	Still living		Dog in good health with normal bowel control	normal bowel control
14	6 wks	Still living		Dog in good health with normal bowel control	normal bowel control
15	3 wks	Still living		Dog in good health with normal bowel control	normal bowel control

the segment of the upper rectum to be cut and the segment with the blood vessel was found to be long enough to reach the perianum (the same as first).

With the abdomen still open and in large of the rectum the rectal segment (1) being the retractor was pulled from below the lower rectum. The mucosa and perianum were lifted and the rectum draped. A transverse incision was then made 2 cm from the anal sphincter through the external rectal wall and the upper segment of lower rectum was pulled down through the pelvis and as with the guidance of the rectum the lower rectum was pulled down from the anal sphincter. The rectum at end of the lower rectum was cut off. The lower rectum was then put back in place and the pelvic peritoneum was sutured and the abdominal incision closed.

After 24 hr the colon was moved. For the four months from then until the time of the next operation there had normal bowel movement without the aid of diet, laxatives or drug therapy.

Operation has been done in two additional similar cases since that time and the patients are doing well two months and three weeks, respectively after operation.

#### DISCUSSION

We feel that this method will be a useful adjunct for the treatment of benign lesions of the rectum and rectosigmoid, such as severe spasm. It may have a place in the treatment of carcinoma. However the work of Westhues

and of Collier and associates tends to show that metastasis from rectal cancer is in an upward direction rather than in a lateral one. This leads us to feel that a selection might be made of small, localized lesions which could be treated by the procedure we have described. Babcock, Bacon, Wangenstein,<sup>10</sup> and Mandl feel that this can be done using, as they do, the same general approach.

In the technique of the operation, the most important step is to be certain that the blood supply to the proximal end of bowel is of adequate length to permit the sigmoid to be pulled out through the anus. It is also important that the anastomosis be done in two layers with extreme care to make sure that there be no leakage into the pelvis.

#### SUMMARY

1. A series of twenty cases of megacolon with spasm of the rectosigmoid in children is reported.

A method of resection of the rectum and rectosigmoid, with preservation of the sphincter is described. This method was evaluated in a series of fifteen dogs. Results showed (a) infection in but one case, (b) good sphincter control in all, and (c) no postoperative strictures.

3. The operation has been successfully used on three children.

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# THE ROLE OF HYPERTROPHY OF THE MUSCULARIS IN THE DELAYED ONSET OF SYMPTOMS IN CANCER OF THE COLON

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RECENTLY my attention was forcefully called to the paucity of symptoms in some cases of cancer of the colon by observing a fellow surgeon in whom this disease progressed to an incurable stage before he was aware of trouble. Although this may not be the usual situation, it occurs with sufficient frequency to justify investigation of some of the factors which make this possible.

An impressive finding in specimens of cancer of the large bowel which exhibit stenosis of the lumen is the thickening of the muscle coat proximal to the obstruction. The extent of the thickening appears to be related to the duration and degree of stenosis. Thus, the development of hypertrophy of the muscle coat is a logical result of increased work demanded of it. The same response occurs in any hollow muscular viscus such as the heart, urinary bladder, gall bladder, stomach, and other organs. The response of striated muscle is also essentially the same when it is subjected to increased activity over a period of time.

Nothnagel observed this hypertrophy of the large bowel and emphasized its importance in interpreting symptoms or lack of symptoms. His student Herzog carried out a series of animal experiments and came to the conclusion that detectable hypertrophy resulted from incomplete obstruction after five days, while gross visible hypertrophy was seen in nine days. Hypertrophy and not hyperplasia is the essential change.

Morrison and Sarnt and Osgood have discussed the principle of muscle hypertrophy and compensation as it applies to stenoses in hollow viscera. A careful search of the literature has failed to reveal other significant or recent contributions on this subject. In fact, no reference to this concept is made in textbooks and standard works on medicine and surgery. This concept appears to be of fundamental importance and yet it has either been forgotten or regarded as of only academic interest for many years.

There are well known differences in the physiology of the right and left segments of the colon as well as certain differences in the types of tumors originating in these structures. However, in practically all cases of cancer of the left colon and in many in the right colon some interference with the normal transit of bowel content develops. The first symptom produced are therefore related to partial obstruction.

If the mechanical aspect of the problem are considered, several adjustments may be made to overcome or minimize the effect of partial obstruction. Among these probably the most important are increased propulsive power of the bowel wall resulting from hypertrophy of the muscle coat, decreased resistance to the passage of stool, the lubricating effect of increased mucous secretion



and, rarely an increase in the caliber of the area of stenosis by sloughing of the tumor. In addition, the patient or the physician may supply certain compensatory factors, such as changes in the diet which tend to lower the residue in the stool lubricating or laxative medicaments, enemas, and antispasmodic drugs.

Thus, in the bowel as in the heart compensatory mechanisms for overcoming the deleterious effects of stenosis exist, and the lesion may remain partially or completely silent. Unfortunately however the course of cancer is progressive and, as obstruction increases, the limits of compensation are reached. At this time unequal local symptoms of serious trouble appear and often the lesion is a far advanced one.

While any or all of these mechanisms may come into play it is entirely conceivable that muscle hypertrophy with resultant increased propulsive power alone may completely or partially mask the symptoms of increasing obstruction for many months. Changes in bowel habits, abdominal cramps, distention, and the vague feeling of fullness of which these patients so often complain are manifestation of partial obstruction. Since these symptoms may not be significant until compensation begins to fail, neither the patient nor the physician can await their appearance of universal early detection is hoped for.

If symptoms cannot be relied upon to indicate early lesions, how then can early cancer of the colon be detected? Although this problem is beyond the scope of this paper it appears that the answer must be found in the education of the public and the physician alike. This would require periodic investigation of those organs susceptible to cancer under and more frequent use of the means for studying these organs, and an appreciation of Von Mikulicz's laudable statement that there are no symptoms of cancer but only symptoms due to the complication of the disease.

During the past year about twenty unselected cases of cancer of the large bowel have been studied. Specimens were examined in the fresh state however measurements of the thickening of the muscular wall were not recorded except in some instances. The specimens removed have necessarily been of limited extent and it has not been possible to determine how far proximal or distal to the tumor changes in the wall existed. These problems require further study.

Inspection of the specimens revealed gross thickening of both the circular muscle layer and the longitudinal lines. This thickening is most marked in the proximal bowel and increases as the tumor is approached. Below the tumor there is also some increase in the thickness of the muscle wall, but this is of less degree. The muscle layers stand out clearly in both the fresh and fixed specimens, and comparisons were made with specimens removed at necropsy from individuals with no disease of the colon (Fig. 1).

All roscopic sections were taken through the wall both proximal and distal to the tumor. In most instances, blocks were cut transversely at a distance of 5 cm. from the tumor margin. Characteristic histologic changes consistent with hypertrophy of smooth muscle cells were noted.

The muscle layers were increased in thickness, and there was no evidence to indicate that edema or cellular infiltration was responsible for this change.



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Inspection of the specimens revealed gross thickening of both the circular muscle layer and the longitudinal lines of the proximal bowel and increases as the tumor is approached. In the distal bowel there is also some increase in the thickness of the muscle layers.

The muscle layers stand out clearly in both the fresh and fixed specimens, and comparisons were made with specimens removed at necropsy from individuals with no disease of the colon (Fig. 1).

Microscopic sections were taken through the wall both proximal and distal to the tumor. In most instances, blocks were cut transversely at a distance of 5 cm. from the tumor margin. Certain characteristic histologic changes consistent with hypertrophy of smooth muscle cells were noted.

The muscle layers were increased in thickness, and there was no evidence to indicate that edema or cellular infiltration was responsible for this change.

The specimen showed a large annular obstructing adenocarcinoma of the sigmoid, involving all layers of the bowel wall. There was dilatation and very marked muscle hypertrophy above the lesion (Fig. 3) and marked hypertrophy below. The mesenteric nodes were not involved.

Case — M. B. 56-year-old woman was admitted to the hospital on Nov. 1947, complaining of constipation for one year. There had been no abdominal pain, discomfort. Cathartics had been taken 10 times as frequently. Blood in the stool thought to be due to bleeding piles, had been noted for several years. Weight loss was fifteen pounds.



Fig. 3 — (A) Gross longitudinal section of the sigmoid adenocarcinoma showing obstruction of the lumen. (B) Photomicrograph of the tumor tissue. (C) Photomicrograph of the tumor tissue showing cellular details. (D) Photomicrograph of the muscularis propria showing marked hypertrophy of the muscle fibers.

The abdomen was distended and diffusely tender. A mass was felt in the left lower quadrant. Rectal examination was negative. A flat plate of the abdomen showed distention of the colon. At operation, perforated obstructing carcinoma of the sigmoid colon was found, and colostomy was performed. Subsequently, resection of the sigmoid with end-to-end anastomosis was carried out, and later the colostomy was closed. Convalescence after the first procedure was stormy, but the eventual outcome was satisfactory.

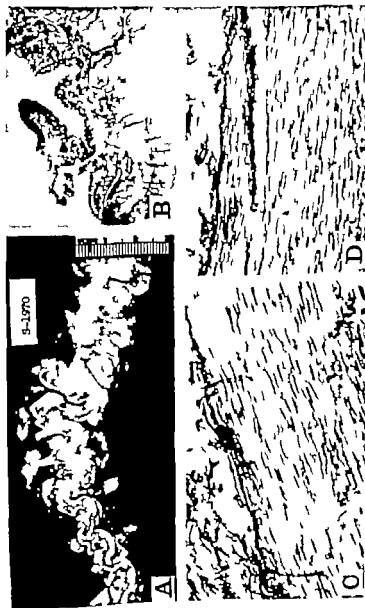
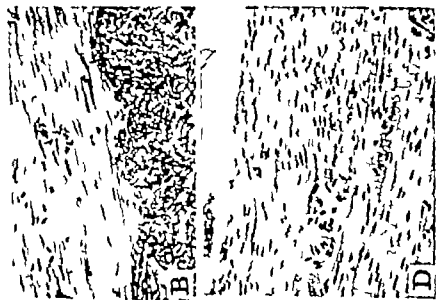


Fig. 1—Sections from Case 2. (A) Low magnification view of the tumor. (B) Higher magnification view showing glandular structures. (C) High magnification view showing cellular details. (D) High magnification view showing cellular details. The tumor is a well-differentiated adenocarcinoma of the colon. The glandular structures are well formed and the cells are uniform in size and shape. The nuclei are small and round, and the cytoplasm is scanty. The stroma is fibrous and contains many inflammatory cells.

The specimen showed large annular retracting demarcate zones of the sigmoid, in which all layers of the bowel. There was dilatation and ery marked muscle hypertrophy above the lesion (Fig 3) and milder hypertrophy below. The mesenteric nodes are not involved.

CASE - M R 50 yr old male, admitted to the hospital on Nov 194 with  
planning of constipation for one yr. There had been no abdominal pain or discomfort  
Character had been taken in increasing frequency. Blood in the stool, thought to be due  
to bleeding piles, had been noted for over 1 yr. Weight loss fifteen pounds.

[illegible]

The examination again swept for tenderness in the left lower quadrant. A firm mass revealed an obstructing lesion in the sigmoid.

A resection of the sigmoid with end to end anastomosis was performed. Cantharidin was unavailing.

The specimen showed a sessile polypoid, sclerotic adenocarcinoma almost completely obstructing the lumen. There are no metastases to the mesenteric nodes. The bowel wall above the lesion showed marked hypertrophy of the muscle and slight hyperplasia (Fig. 4).

Case 3—E. B., 32-year-old man, was admitted to the hospital on May 1, 1947. For six months prior to admission, this patient had had loss of bowel bowel movement. Two weeks before admission there had been cramping lower abdominal pain and some distention. These symptoms lessened and he felt well until ten days before admission, when symptoms of complete colonic obstruction appeared. There had been no blood noted in the stool, nor had there been weight loss or other significant symptoms.

The abdomen was distended and there was tenderness in the left lower quadrant. Radiographic studies confirmed the impression of obstruction of the sigmoid. Sigmoidoscopic examination was negative.

Conservative measures resulted in decompression, and later sigmoid resection with end to end anastomosis was carried out.

The specimen showed an sessile adenocarcinoma protruding beyond complete obstruction of the lumen. There was invasion of the muscle and serosal layers of the bowel wall. Lymph node metastases were noted. Proximally to the lesion the muscularis thickened. Distally there was some hypertrophy but not marked as there was proximal to the lesion (Fig. 1 C).

Confinement was unavailing until May 4, 1947, when left lower quadrant cramping appeared. A mass could be felt in this area, and barium studies demonstrated narrowing in the descending colon. Later it was found that the narrowing was probably from growth of secondary lesions.

A laparotomy, second primary lesion rising from the descending colon but adherent to the distal transverse colon and greater curvature of the stomach was encountered. There were no apparent metastases. En bloc resection of the involved colon, including the splenic flexure and mesentery, the omentum and portion of the greater curvature of the stomach was done. An end to end anastomosis was not possible. Confinement was unavailing, but progress was guarded.

This specimen revealed primary adenocarcinoma of the descending colon, with partial obstruction of the lumen of the lesion and partial obstruction of the lumen of the previous anastomosis which was 12 cm below the second lesion. The infiltration of the stomach and transverse colon involved the superficial layers only. There were no involved lymph nodes found. Muscular hypertrophy was below the lesion and above the anastomosis was marked.

Case 4—H. D., 47-year-old man, was admitted to the hospital on April 26, 1947, complaining of abdominal cramps, constipation, drowsiness and abdominal distention of three weeks duration. Traces of blood had been noted in the stools for about ten and one-half years.

The abdomen was distended and firm. Tenderness was localized to the left lower quadrant. Rectal and sigmoidoscopic examination were negative. A distal part of the ileum and terminal caecum revealed an obstructing lesion of the sigmoid.

A transverse colectomy was established on the day of admission. Later resection of the sigmoid with end to end anastomosis was performed. There was no gross metastases. Confinement was complicated by postoperative ileus. The resection was unilaterally limited.

The specimen revealed an sessile constricting adenocarcinoma, a complete obstruction and deep invasion of the bowel wall. Metastases to the lymph nodes were found. The muscle layer was greatly thickened.

Six months later the patient exhibited signs of peritonitis, namely in the pelvis, in involving the colon and bladder.

CASE 5—E. H. 40-year-old man, was admitted to the hospital on Oct. 1947 complaining of cramping abdominal pain for best one and one-half years. The cramps or associated with bowel movements and occurred in the morning at the usual time of defecation. There had also been some cramping pain on urination. Constipation appeared three months prior to admission, and he had learned that evacuation took longer and the stool was of smaller caliber than normal.

The examination was negative except for mass which could be felt per rectum but could not be seen through the sigmoidoscope. Barium enema revealed an obstructing lesion at the mid sigmoid.

A resection of the sigmoid with end to end anastomosis was performed. Curectomy was not performed.

The specimen showed an angular adenocarcinoma, constricting and obstructing the lumen. There were involved mesenteric nodes present. The muscle coat was markedly thickened above the tumor and moderately thickened below.

CASE 6—W. B. 43-year-old man, was admitted to the hospital on Aug. 30 1947 complaining of increased constipation for 6 months and blood in the stool for 2 weeks. There had been decrease in the caliber of the stool and frequent loose bowel movements after taking laxatives. No pain had been noted.

An obstructing, ulcerated mass was found at 12 cm. on sigmoidoscopy. This proved to be carcinoma on biopsy. A tervor resection with end to end anastomosis was performed. Curectomy was not performed.

The specimen showed an annular partially obstructing lesion. A lymph node involvement as found. The muscle layer of the bowel proximal to the tumor showed moderate hypertrophy, there was no central lumen distally.

CASE 7—A. E. 50-year-old woman, was admitted to the hospital on Sept. 9 1947 complaining of constipation and blood in the stool. Two months prior to entry mild constipation requiring laxatives had been observed. In addition, the patient was conscious of increased distention and recent water blood in the stool. For three weeks there had been mild lower abdominal cramps.

An obstructing lesion of the descending colon was found on barium study. A subtotal type of resection was performed. The subsequent course of the colostomy ileostomy was unsuccessful.

The specimen showed an angular keratinizing adenocarcinoma of the colon with extension through the bowel wall. There were several nodes in the lymphatic nodes. A moderate degree of hypertrophy of the muscle coat was present above the lesion.

#### DISCUSSION

It appears that those cases in which symptoms did not appear until late in the course of the disease exhibited the greatest degree of muscle hypertrophy. Thus, the patient (Case 1) who had the most marked thickening of the muscle coat of any of the specimens examined had no symptoms until two days before admission to the hospital. Two others (Cases 3 and 4) showed marked hypertrophy and were relatively free of symptoms until admitted with acute obstruction. On the other hand, there were two patients (Cases 6 and 7) who had constipation and bleeding of relatively longer period and showed only moderate hypertrophy. This is probably insufficient to compensate fully for the constipation which the patients exhibited. It is probable that rapid growth plus associated inflammatory changes and resultant stenosis may prevent adequate compensation in producing distention of the proximal bowel sufficient to inhibit activity in the viscero-splenic reflex and hence retard the normal stimulus to hypertrophy.



One patient (Case 6) had had recurrent abdominal cramps for one and one half years with constipation superimposed for ninety days. What is the significance of this sequence of events? It would seem that the cramping pain represented an attempt on the part of the bowel to compensate for a very slowly developing stenosis. Certainly the cramps must have resulted from increased peristaltic activity since they always occurred just preceding and during evacuation. Later in the course of the disease, as compensation began to fail, constipation was observed and the patient resorted to laxatives to aid the overtaxed bowel. In spite of the apparent embarrassment to effect a peristalsis produced by the tumor the response in the form of hypertrophy was only moderate.

Each of these cases showed some degree of hypertrophy of the muscle layer proximal to the stenosing carcinoma. The duration and severity of symptoms in these cases suggest an inverse ratio to the degree of hypertrophy in those lesions progressing to almost complete obstruction.

#### SUMMARY AND CONCLUSIONS

1 The large bowel like other hollow muscular viscera, has the ability partially or completely to compensate and overcome at least temporarily the adverse effects of a slowly developing stenosis, such as occurs in carcinoma.

The most important factor in the compensation mechanism of the large bowel is hypertrophy of the muscle coat.

2 As obstruction increases and the limit of hypertrophy is reached, a stage of decompensation results and symptoms may appear at this time.

3 The compensation mechanism may operate to delay onset of significant symptoms until curative surgery is no longer possible.

4 The usual symptoms, which are changes in the bowel habit, abdominal cramps, and appearance of gross blood in the stools, cannot be entirely relied upon to indicate the need for investigation of the colon.

The writer wishes to acknowledge his assistance of Vernon D. Swenson, M.D., Department of Pathology, University of Oregon Medical School, Portland, Ore., Herbert H. Foster, M.D., Pathological Diagnostic Hospital, and H. Mueller, M.D., Pathologist, Proctor Hospital, Portland, Ore., in this study.

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## THE INDICATION FOR EMERGENCY OPERATION IN SEVERE HEMORRHAGE FROM GASTRIC OR DUODENAL ULCER

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THE availability of large quantities of blood for emergency use has influenced the treatment of severe upper gastrointestinal hemorrhage and makes it desirable to re-evaluate the place of emergency operation for this condition. The poor results of emergency surgery in the past, contrasted with the supposedly good results of nonoperative management have led in many hospitals to the belief that such cases are medical and the surgeon is to be called in only at the last minute (if then) to perform a hasty procedure upon a nearly moribund patient. This plan has found apparent justification in the past on the basis that the overall mortality from bleeding ulcers has been less than the small mortality from gastric operations. There can be no quarrel with the demonstrable fact that the vast majority of patients who bleed from the upper gastrointestinal tract will get well with conservative measures. More over emergency operation for bleeding peptic ulcer may be one of the most harassing and difficult in the entire surgical domain. But it is likewise a lesson in the fact that some patients will die without operative intervention, and it is our contention that a larger proportion of them may be salvaged by timely surgery.

If one accepts the fact that some patients who would otherwise die can be saved by emergency operation there are two alternative approaches which suggest themselves. One is to operate at once upon every patient in whom there seems to be any possibility, however remote, that the hemorrhage may prove fatal. This attitude will necessarily result in some needless operations under difficult circumstances. The other approach is to limit emergency operation in so far as possible to those patients who actually seem to be bleeding to death. We have adopted the latter view since it is of sound logic for the patient to have an unnecessary gastric surgery performed, if possible, in a quiet environment.

The crux of the matter of course lies in the accuracy of the selection of patients for operation. It is our belief that the chief problem is the fact that many of the factors which govern the outcome on conservative management rather than the age of the patient, the number of previous hemorrhages, and other factors which have usually attracted attention in the past. We have adopted the following rule as a basis for recognizing promptly those patients in whom the rate of blood loss is sufficiently rapid to make spontaneous recovery unlikely. Briefly stated this limit rule is as follows: (1) the rate of bleeding such that stable respiration cannot be maintained with transfusions roughly approximating 1 unit of blood per twenty-four hours,

spontaneous cessation of the hemorrhage is unlikely and emergency operation should be undertaken.

A prerequisite for emergency surgery in upper gastrointestinal hemorrhage is a knowledge of the source of the bleeding. Although roughly 75 per cent of these hemorrhages arise in gastric or duodenal ulcers, it must be recalled that approximately 20 per cent come from such lesions as esophageal varices or gastritis which are not amenable to emergency operation. Another 4 or 5 per cent are due to gastric neoplasms in which prompt surgery is necessary since there is no hope of healing the ulcer by dietary means. If the source of the bleeding is not evident from the history, clinical findings, and previous roentgenograms, an x-ray examination of the esophagus, stomach, and duodenum should be done prior to emergency operation. The demonstration by Hampton and Schatzki that this can be carried out with comparative safety in a patient who is actively bleeding is a contribution of great value to the surgeon and should serve to help us avoid an operation upon patients who cannot possibly benefit by one. If a surgical lesion cannot be demonstrated by these means, it is wiser to withhold surgery.

In a previous communication with Gray we have recorded our experience with bleeding peptic ulcer at the Peter Bent Brigham Hospital since 1940. It was shown that when the cases were divided according to the severity of the hemorrhage into four groups arbitrarily designated as moderate severe compensated, severe uncompensated and exsanguinating hemorrhage the fatalities with two exceptions were in the exsanguinating group. These two fatalities were ascribable in one case to coexistent heart disease and in the other to an operation for which the patient was badly selected and poorly prepared. Those patients classified as having moderate hemorrhage occasionally had syncope or fainting at the onset but without exception they entered the hospital in a stable circulatory state and gave little evidence of continued bleeding. The hematocrit level ranged between 31 and 40. Blood transfusions were unnecessary.

The second group with severe compensated hemorrhage was characterized by more prolonged bleeding with uterine shock, hypotension. Repeated melena was usual and occasionally there was hematemesis, abdominal distention, and anorexia. The estimated rate of bleeding in this group was 500 to 1,000 cc per day but the pulse rate and blood pressure remained comparatively stable and the principal indication for transfusion were continued melena and falling hematocrit. Spontaneous recoveries in this group, as in the foregoing one, is the rule and patients in the group may be dismissed from further consideration as candidates for emergency operation.

Patients in the next two groups of severe uncompensated hemorrhage and exsanguinating hemorrhage are the ones that demand the most critical evaluation. Patients in both groups give evidence of shock. The response to therapy and particularly to blood transfusion ultimately serves to differentiate the two groups from each other. We strongly advocate that all patients who are in shock at the time of hospital admission, subsequently develop

evidence be closely followed by a bedside team of both internist and surgeon. In fact, we believe that such patients could be placed to advantage on the surgical wards, as are their patients who are potential candidates for any type of emergency operations. Patients with severe uncompensated hemorrhage are bleeding at an estimated rate of 1,000 to 1,500 cc per twenty-four hours. They may require as much as 1,000 to 2,000 cc of blood within the first few hours of hospital admission to stabilize the circulation, and they may continue to bleed actively for several days after treatment has been started. However, despite repeated hematemesis or gross bloody stools, they do not again develop syncope, shock, or marked hypotension provided that they are given transfusion at rates of about 500 cc of blood every eight hours. If at any time after initial stabilization of the circulation and under such a transfusion regime, syncope, shock, or merely a sharp rise in the pulse rate or lowering of the blood pressure occurs the patient is considered to be in the exsanguinating group.

Patients with an exsanguinating hemorrhage are in a very precarious situation and we have come to believe that operation is safer for them than expectant management with even more rapid rates of transfusion. The estimated rate of bleeding is more than 1,000 cc per twenty-four hours. An exsanguinating hemorrhage may manifest itself in one of several ways. Some patients are admitted in profound shock and respond slowly to the usual rate of transfusion, tending to re-entrant shock soon after each bottle of blood is finished. An occasional patient will respond fairly well to the initial transfusion but will slowly and definitely lose ground over a period of several days. Some will show an apparent initial arrest of hemorrhage only to be followed by the sudden development of syncope or shock, giving evidence of very rapid, if intermittent, bleeding. In these last patients particularly a prompt intervention is recommended, even if several days have elapsed since the onset.

It has been said that in dealing with a bleeding ulcer the patient should be given transfusions vigorously until the circulation is stable and then at the first sign of further bleeding operation should be performed. We disagree with this view. If the circulation cannot be stabilized after the initial hemorrhage by transfusion of not more than 1,000 cc of blood, transfusions should be continued and operation performed as soon as the circulation is stabilized. If the initial response to transfusion is good, operation should not be performed at the first sign of further bleeding unless the rate is sufficiently fast to produce syncope or a break in the pulse rate or blood pressure by its transfusion at a rate of approximately 500 cc every eight hours.

A patient, therefore, with upper gastrointestinal bleeding who is in shock on admission to the hospital, or who develops evidence of it under treatment, must be followed not only with the customary pulse and blood pressure recordings, preferably at half-hourly intervals or less, but also repeated clinical examination and a determination of the hematocrit (or its equivalent) every eight hours, day and night. Every means of control must be utilized

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A patient therefore with upper gastrointestinal bleeding who is in shock on admission to the hospital, who develops evidence of it under treatment must be followed not only with the customary pulse and blood pressure recordings, preferably at half-hourly intervals or less, but also repeated clinical examinations and a determination of the hematocrit (or its equivalent) every eight hours, day and night. Every scrap of evidence must be utilized

In an effort to determine whether or not the patient is actually holding his own when he receives approximately one pint of blood every eight hours.

In Fig 1 is shown the course of a patient whose hemorrhage has been classified as severe uncompensated, but which almost falls into the exsanguinating group. She received insufficient blood during the first three days of the hospital stay (and it may be said parenthetically that this was a

### BLEEDING DUODENAL ULCER

E.D. Severe Uncompensated

7,250 cc blood in 9 days

F. male Ag. 65

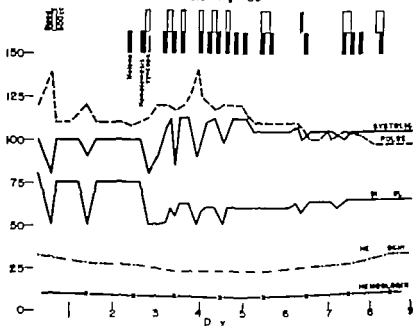


FIG. 1

The patient not seen by the gastrointestinal team during these first three days. The pulse was very normal and the blood pressure fluctuated as much as 10 or 15 points and tended to stabilize below the normal level. However, it was maintained near that level despite continued hemorrhages and melena, although transfusion later on at the rate of 1,000 to 1,500 cc daily were required. When the pulse rose to 140 on the third day, accompanied by a drop in blood pressure an operation would have been indicated if the favorable response to the single transfusion administered at that point had not been maintained.

In Fig 2 is shown the course of an exsanguinating hemorrhage. This patient was unusual in that he was coming from the closure of a perforated gastric ulcer five days previously when bleeding began. He was in shock when he received the first transfusion, but responded well to 500 cc.

Within a few hours he became weak and faint, and a break showed in the temperature chart again he responded well to a single transfusion. In another few hours he once more gave clinical evidence of rapid bleeding and when after an additional liter of blood the circulation was not yet stable the rate and volume of transfusion were increased, and gastric resection was performed. He made an uncomplicated recovery.

### BLEEDING DUODENAL ULCER

WB Exsanguinating 3000 cc. blood in 1 day

Male Age 35

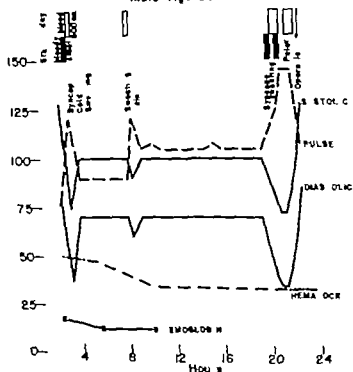


FIG. 2

FIG. 3 is another example of the course of an exsanguinating hemorrhage. In this instance the patient entered the hospital in collapse but responded rather quickly to a single transfusion of 500 cc. of blood. Later that day he had a sharp fall in blood pressure and rise in pulse which again responded to a single transfusion. The exsanguinating nature of the hemorrhage became obvious when an additional liter of blood a few hours later failed to stabilize the circulation. Operation was performed, and the bleeding vessel in the duodenal ulcer bed was transfixed. This is ordinarily not a procedure to be recommended unless accompanied by complete diversion of the gastric content because of the danger of secondary hemorrhage. In this instance however the patient recovered.



As stated before we believe that the rate of bleeding takes priority over the age of the patient in the decision to operate. The importance of age lies in the fact that older patients are more prone to develop an exsanguinating hemorrhage than younger ones (Table I). When age is considered in relation to the severity of the hemorrhage it can be seen that in this series, the differences between young and old are not marked. There was a high proportion of fatal hemorrhage in the exsanguinating group irrespective of age and a low mortality in the other combined groups. In fact, if the two cases already alluded to earlier in the paper are excluded, the only deaths were in the exsanguinating group. Thus, it may be seen that many patients over fifty

### BLEEDING DUODENAL ULCER

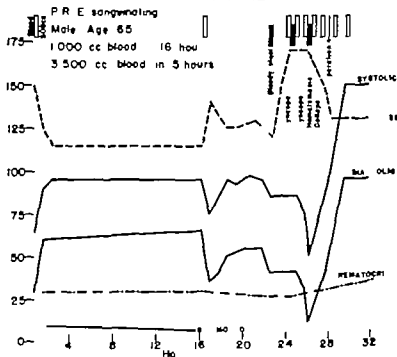


FIG. 3

years of age would be subjected to unnecessary operation if the factor of severity were not considered and conversely that patient under 50 years can and do die when an operation might have saved them. It is likewise logical not to be bound to a hard and fast rule concerning the duration of the hemorrhage if a sound indication for operation should make its appearance three or four days after bleeding commenced. We have operated successfully upon patients who suddenly bled again with great severity after several days of quiescence, and we feel strongly that for such patients, especially an operation is proper even though the risk is admittedly great.

TABLE I ACUTE HEMORRHAGE FROM ULCER,  
A. & B. MORTALITY (1940 TO 1947)

TYPE OF HEMORRHAGE	AGE (Yr.)	CASES	DEATHS
Exsanguinating	50 or more	8	6
	49 or less	6	2
Moderate	50 or more	60	—
Severe compensated	49 or less	5	0
Severe uncompensated			

In Table II may be seen the comparison of the results of treatment at the Peter Bent Brigham Hospital during the last two years (1946 and 1947) and during the preceding six years (1940 through 1945) when there was no systematic approach to the problem. Although the series is too small for statistical significance the trend is in the right direction. The only fatality in the last two years was an elderly diabetic patient who entered the hospital in shock and who died before effective treatment could be instituted. Moreover a critical review of the fatal cases in the preceding period has convinced us that several of the patients might have been saved if they had been treated according to our present plan.

TABLE II DEATHS FROM ULCER, PETER BENT BRIGHAM HOSPITAL

TYPE	TREATMENT	1940 TO DEC. 1945		1946 TO DEC. 1947	
		CASES	DEATHS	CASES	DEATHS
Moderate	Medical	15	—	17	—
	Surgical	—	—	—	—
Severe compensated	Medical	35	1	16	—
	Surgical	1	1	—	—
Severe uncompensated	Medical	13	—	10	—
	Surgical	1	—	1	—
Exsanguinating	Medical	6	6	—	1
	Surgical	3	—	1	—
Total		117	9 (7.6%)	43	1 (2.3%)

Table III lists the operations performed for massive upper gastrointestinal hemorrhage in the two periods just considered. The series is small, but the fact that there have been no deaths in seven operations in the past two years is sufficiently encouraging to warrant some holders in recommending emergency surgery for the suitable case.

TABLE III EMERGENCY OPERATION FOR UPPER GASTROINTESTINAL HEMORRHAGE

TYPE OF CASE	1940 TO 1945		1946 TO 1947	
	CASES	DEATHS	CASES	DEATHS
Emergency & critical	4 (3 gastric, 1 gastr.)	0	4 (3 gastric, 1 gastr.)	0
Quiescent	1 (gastric)	—	1 (gastric)	0
Quiescent	—	—	1 (gastric)	0
Total	5	0	6	0

Location found only in two operations

# DISCUSSION

It is suggested that the principal criterion to be employed as an indication for emergency operation in severe upper gastrointestinal hemorrhage is the

rate of bleeding. If a patient is in shock on arrival at the hospital, or develops evidence of it while under treatment, he deserves the constant vigilance of a bedside team of internist and surgeon, and is preferably treated on the surgical wards. If the hemorrhage does not seem to be controlled with blood transfusions approximating 500 cc every eight hours, an emergency operation is to be considered seriously. An exact knowledge of the source of the bleeding determined by emergency x-ray examination if necessary is a prerequisite of this type of surgery in order to prevent a useless operation.

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Obst (in press)

## MASSIVE HEMORRHAGE FROM GASTRODUODENAL ULCER

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WILLIAM H POTTER, M D AND SIDNEY M SCHAFER, M D  
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(From the University of Buffalo Medical School and the Edward J Meyer  
Memorial Hospital)

THERE are various reasons why the management of the severely bleeding gastric or duodenal ulcer has been a subject of controversy and doubt. Two major factors have been incomplete description of the cases under consideration and variable quality of the non-surgical or surgical treatment given. In other words both the case material and the treatment under discussion were often uncertain. Other sources of confusion readily apparent in a study of the literature are too small a series of cases, errors in diagnosis, and a tendency of the proponent of a particular method to attribute deaths to associated diseases rather than to hemorrhage and anemia.

In view of the recent advances in surgical technique, improved knowledge of how to treat hemorrhagic shock, and better anesthesia it would seem that the advantages of early surgical treatment of bleeding peptic ulcer deserve more serious consideration than in the past. Accordingly since January 1941 an effort was made on our surgical service to evaluate a plan of management of acutely bleeding gastric and duodenal ulcers involving immediate blood replacement and early subtotal gastric resection. The study is still in progress and final conclusions are not yet in order although sharp impressions are taking shape in the minds of those engaged in the work. The purpose of the present report is presentation of the plan of management being used and analysis of laboratory and clinical data acquired to date.

We define acute massive hemorrhage as hemorrhage grossly manifested by vomiting of blood, or tarry stools, with faintness, pallor or loss of consciousness within one week of admission to the hospital. By early surgical treatment is meant gastric resection with removal of at least 80 per cent of the stomach within twenty-four hours of admission to the hospital. The only patients with acute massive hemorrhage into the upper gastrointestinal tract not operated upon are those refusing operation, those presenting strong evidence of primary blood disease with a lotting defect or those with evidence of cirrhosis of the liver with esophageal varices. In case of reasonable doubt as to the source of bleeding exploratory laparotomy is performed immediately (within twenty-four hours). When the site of bleeding cannot be determined by laparotomy and there has been vomiting of blood or tarry blood in the stomach or duodenum subtotal gastric resection is performed nevertheless.

Laboratory measurements including determination of blood volume and extracellular fluid volume are made by a trained team within one-half hour



Four of the patients operated upon died and two of those not operated upon died. Brief summaries of the fatal operative cases follow:

1. *Pe* a 74-year-old man, was admitted to the hospital in coma, with incontinence of urine and feces, and died twenty-four hours after operation. Autopsy showed cerebral softening probably due to anoxia.

2. *Ar* a 46-year-old man, died six days after operation, with vomiting and diarrheal movement containing blood. Severe pulmonary atelectasis was noted before death. No autopsy was done.

3. *Ki* a 68-year-old man died suddenly three days after operation probably of coronary occlusion. He had recently been treated for cardiac failure. No autopsy was performed.

4. *Po* a 61-year-old hunchbacked man with a severely deformed chest cavity 1 month and gasping for breath. He died seven hours after operation, autopsy showing cor pulmonale, coronary atherosclerosis.

The two patients who died without operation are briefly described as follows:

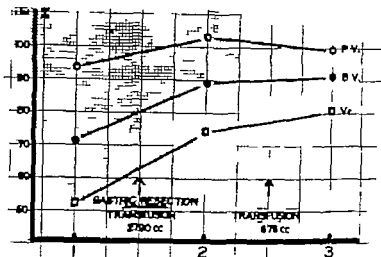
1. *Pr* a 67-year-old man refused operation and died suddenly fourteen days after admission, probably of coronary occlusion. No autopsy was done.

2. *Ch* a 33-year-old man, entered the hospital in hemorrhagic coma and died four hours after admission despite the administration of 2,500 c.c. of blood. Autopsy developed a posterior wall duodenal ulcer involving only the duodenal mucosa and submucosa as the source of bleeding.

As seen in Table I these patients for the most part fell into the older age group. The severity of hemorrhage is attested by the average values for red blood cell count, hemoglobin, and blood volume before treatment. Blood volume and hemoglobin values were found to be reduced much more than plasma volume and plasma protein values. This finding emphasizes once more the fact that the critical element in severe hemorrhage is reduction in hemoglobin and oxygen carriage and not depletion of the plasma.

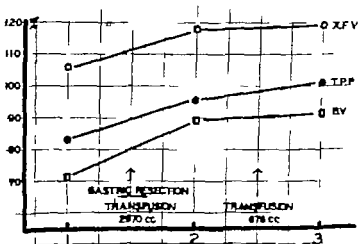
In Fig. 1 the relationship between blood volume, plasma volume, and hematocrit in terms of average values for the seventeen patients operated upon for gastric or duodenal ulcer is indicated. The observations at Point 1 were made within one-half hour of admission; those at Point 2 were made within twenty-four hours of admission during which time gastric resection and blood transfusion in the average amount of 2,790 c.c. had been carried out; the observations plotted at Point 3 represent average values after an average interval of eleven days following operation. The average amount of blood administered during the period of observation was approximately 35 liters. Nevertheless, hematocrit values and blood volume were still somewhat below normal in convalescence. In fact in none of the seventeen patients was there any evidence of overtransfusion. In two instances iron toxicity and mild jaundice was observed.

Fig. 1 is based on small observations of extracellular fluid volume, total circulating plasma protein, and blood volume from seventeen operative cases. The principal feature is the evidence of supranormal average values for interstitial fluid volume at the three points of measurement. This finding supports



AVERAGE VALUES FOR BLOOD VOLUME (BV), PLASMA VOLUME (PV) AND HEMATOCRIT (Vc) IN PERCENT OF NORMAL IN PEPTIC ULCER WITH MASSIVE HEMORRHAGE

Fig. 1



AVERAGE VALUES FOR EXTRACELLULAR FLUID VOLUME (XPFV) TOTAL PLASMA PROTEIN (T.P.P.) AND BLOOD VOLUME (BV) IN PERCENT OF NORMAL IN PEPTIC ULCER WITH MASSIVE HEMORRHAGE

Fig. 2

conclusions previously reported in an experimental investigation of the acute hemorrhagic state. It raises interesting questions as to the physiologic adjustments of body fluid in the oligemia of acute blood loss. Considerable movement of water and electrolyte from fixed tissue cells, the largest store of water and base in the body with consequent shrinkage in cell volume are involved.

In Fig 3 appear graphically average values for plasma protein concentration, red blood cell count, and hemoglobin concentration in the seventeen operative cases, in terms of per cent of normal. The severity of the hemorrhagic anemia and the large amounts of blood given without overcorrection are demonstrated. The maintenance of normal plasma protein concentration despite grave hemorrhage presumably evidences a greater physiologic reserve of plasma protein than of hemoglobin and red blood cells. In this connection it should be remembered that these patients were in good nutritional state prior to the sudden hemorrhage. In a previously malnourished or cachectic patient the mobilization of plasma protein might be less adequate.

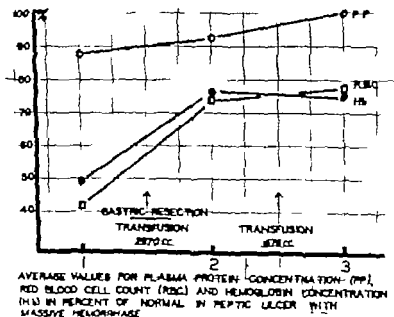


FIG. 3

A consistent finding in analyzing the hemorrhagic state of these patients before and after blood resitution was the failure to achieve quantitative improvements in blood values after giving measured amounts of blood. In Fig 4 this point is illustrated. The data represent average values from seven patients undergoing subtotal gastric resection for acutely bleeding ulcer and all were patients in whom it was possible to be reasonably certain that no further bleeding occurred. The blood loss at operation was measured and averaged 450 cc correction for which has been made in the computations. The blood given the



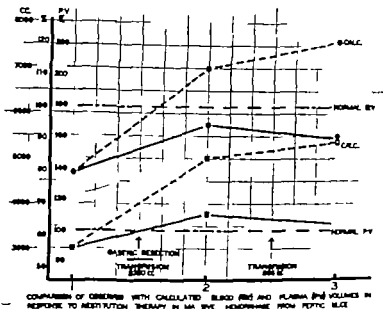


Fig 4

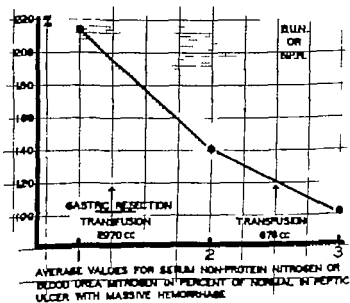


Fig 5

patients was carefully weighed and its hemoglobin and plasma protein content were determined by actual analysis beforehand. A large discrepancy is visible between the observed volume of blood and plasma after transfusion, compared with the expected result. In theorizing on this point, presumably an acute severe hemorrhage leads to shifts of hemoglobin and plasma protein from depots outside the circulating blood with inflow into the capillary bed. Such loans, of lifesaving significance, evidently bear a high rate of interest and are repaid preferentially as physiologic stress is relieved. If this be the case, not only does the phenomenon illustrate a safety factor in the adjustment to blood loss, but also a wide margin of safety in blood replacement. It is probable that clinicians in the past have very generally underestimated the amount of blood lost in acutely bleeding peptic ulcer and have failed to realize that an observed red blood cell count of 2.5 million per cubic millimeter, for example, demands large amounts of blood in restitution. Quarts rather than pints should be considered the unit for transfusion in such patients.

Fig. 3 shows the well known azotemia associated with severe gastrointestinal hemorrhage, average values for seventeen cases being shown. The rapid reduction in plasma nonprotein nitrogen values in twenty-four hours (between Point 1 and Point 2) indicates absence of renal damage and suggests that oligemic impairment of renal blood flow was chiefly responsible for the nitrogen retention. Incidentally it is to be noted that in none of the thirty patients studied and given large amounts of blood was there any evidence of renal damage of the type which has been called the "lower nephron syndrome." Whether the routine early administration of sodium bicarbonate was helpful in this regard is open to question.

In summary, data obtained in the management of a group of patients with acutely massively bleeding gastric or duodenal ulcers have been presented. The plan of treatment, which is still under test, consisted of rapid, copious blood replacement and gastric resection within twenty-four hours of admission to the hospital, controlled by careful laboratory studies. Experiences to date suggest that such a policy affords a better prognosis to the patient than does nonsurgical management. In seventeen operative cases, with an initial average red cell count of 2.3 million per cubic millimeter, the average amount of blood given by transfusion was 3.6 liters. The evidence indicates that this was less rather than more blood than needed.

# THE USE OF THE ROUX Y IN EXTENDING THE OPERABILITY OF CARCINOMA OF THE STOMACH AND OF THE LOWER END OF THE ESOPHAGUS

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## INTRODUCTION

A CURE of carcinoma of the stomach and of the lower end of the esophagus by resection is often impossible because of the presence of metastases so far distant from the primary tumor that resection can be only palliative. However, this procedure is so often associated with gratifying temporary results and seems to be so well tolerated by the patient that it is considered to be justifiable.

Not infrequently, however, the possibility of cure is jeopardized not by distant metastases, but by an actual extension of the disease from the primary tumor along the continuity of the gastrointestinal tract away from the tumor. When the bulk of this extension is not great, one may often be unable to detect the presence of this tumor tissue in the adjacent tissue either by touch or by the appearance of the tissue. Failure of cure in such cases as these then is actually a result of inadequate removal of the tumor along with the contiguous structures which it has involved. In other words, this failure may be, and often actually is, a surgical error. Attempts must be made and constantly are being made, to resect a greater extent of tissue in both directions from the tumor so that any undetectable tumor tissue will automatically be removed. With this in mind, Longmire recently urged the more frequent use of total gastrectomy as the procedure of choice even in fairly small carcinomas of the stomach.

## CASE REPORTS

We wish to report in particular two patients whose cure was not achieved because sufficient local tissue was not removed.

CASE 1 (St. L. K. 47487).—A 54-year-old woman, entered St. Luke's Hospital in September 1943, with typical history of dyspepsia and weight loss. Laboratory study showed

After the stomach was freed up, the abdominal esophagus was felt to be smooth, soft, and pliable. The muscularis appeared and was felt to be normal. A resection more or less after the technique recommended by Lahey and Marshall<sup>1</sup> was done, but when the esophageal wall was divided, there was unmistakable evidence of tumor in the esophageal wall, as determined by the resistance to the scissors; palpation of the cut end of the esophagus. In

Read at the meeting of the Society of University Surgeons, New Orleans, La., Jan. 28-31, 1944.  
From the Fourth Surgical Service, St. Luke's Hospital.

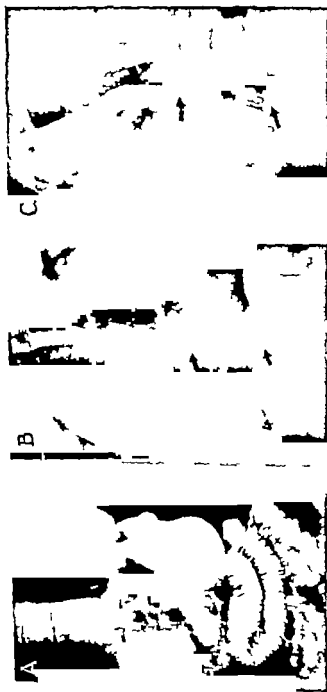


FIG. 1. Case 11. — Photographs showing position of Roux Y after the resection of the stomach. In all of the photographs the Roux Y is indicated by the arrow.

showed the presence of tumor tissue. Because of the patient's age and condition on the operating table the heart was not opened in an attempt to try to remove that portion of the lower esophagus which was involved in the tumor; rather the anastomosis was completed, admittedly in tumor-bearing esophagus, under the full realization that this was not an ideal procedure. Recovery was uneventful.

Microscopic examination of the lower end of the esophagus revealed the presence of gross amount of tumor invading the submucosa of the esophagus. This was definitely adenocarcinoma, not arising primarily in the esophageal wall. Some infiltration of the musculature was seen on high power study (Fig 2).

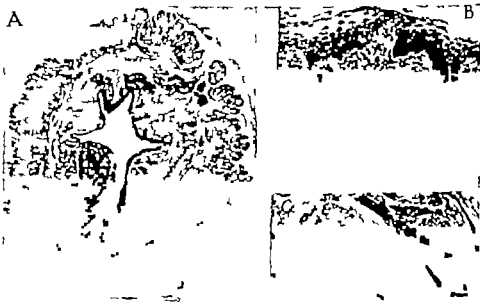


Fig 2 (Case 1).—Photomicrographs of the lowermost portion of the esophagus removed gastrostomically. A: Cross section of the entire esophagus. Note, in particular, the marked infiltration of tumor tissue beneath the mucosa (as shown, enlarged in B). Note also the spread of neoplastic cells in the muscularis of the esophagus (high power shown in C).

14 months later the patient had developed high grade obstruction of the esophagus. She had dysphagia. A biopsy was taken, which showed dense fibrous infiltration immediately beneath the epithelium of the esophagus. No studies showed a filling defect in the esophagus (Fig 1 B and C). She operated upon March 14, 1944, and the esophagus

exposed therapeutically at this time. A mass 4 by 4 cm in diameter extended 10 cm along the length of the lower end of the esophagus. It had both second and third degree invasion of the esophagus. The normal wall of the esophagus appeared to be intact throughout and covered the surface of this mass, which wall appeared to be thin the wall of the

In view of the findings of extensive growth of the reaction of the lower esophagus, the patient was operated upon the peritoneal

CASE (B. & E. N. 11 303).—O. B. entered the hospital July 1, 1941, complaining of dysphagia and weight loss. Examination revealed the presence of a large neoplasm of the

lowermost portion of the esophagus and the upper portion of the stomach. It was impossible to determine the exact site of origin (Fig 3). Through these incisions, the lowermost portion of the esophagus and the stomach were mobilized. The tumor arose from the stomach. Many local lymph nodes and occasional peritoneal metastases made it apparent that the resection would be palliative but we aimed to retain blinking the ability to swallow. The resection and anastomosis were done in the usual manner of Barrett. The postoperative course was unremarkable. The pathologic report however called attention to the presence of carcinoma cells in the submucosal lymphatics of the stomach wall at more than 2 mm. from the cut edge of the stomach (Fig 4). We had been conscious at the time of operation that we were very close to the tumor but did not have the idea that had it proven enough stomach to allow us to bring it up into the chest to reestablish the continuity of the gastrointestinal tract. We had not realized that there was more to be done as the microscopic study showed.



Fig 3 (Case 2).—Preoperative film showing tremendous shortening of stomach caused by carcinoma along the lesser curvature.

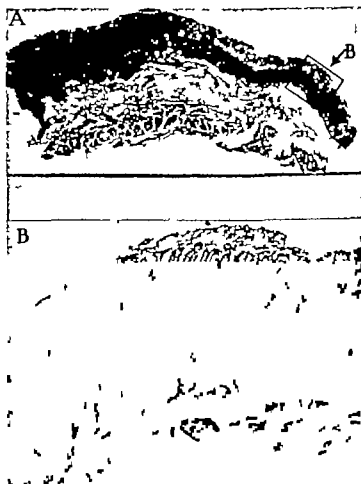
The patient developed some evidence of deglutitory defect four months after the operation. X-ray studies showed some evidence of irregularity of the stomach, which presumed to be local recurrence. The patient died at home in December 1941 of pneumonia. X-ray autopsy was done.

**Comment.**—Both these cases emphasize the fact that palpation and inspection are often inaccurate and are not to be depended upon unwisely in determining the extent of tumor growth. They are therefore inadequate as an available means of deciding the extent to which resection should be carried. It is probable that a microscopic examination of the wall of the gastrointestinal tract at the upper and or lower line of resection will occasionally be necessary at the time of operation to insure against cutting through tumor. In both of these cases such a procedure would have been helpful.

The first case is an example of a gastric carcinoma which invades the adjacent esophagus, a phenomenon which has long been known. The second case illustrates the fact that high lying carcinoma of the cardiac region of the stomach may extend down along the wall of the stomach far beyond the area at which there is palpable or visible evidence of disease.

These experiences make it seem that it may occasionally be necessary to extend the line of our resection farther than either the total gastrectomy as recommended by Longmire or than the esophagogastricectomy as done by Sweet. At the same time we are obliged to attempt to keep the mortality rate of such admittedly formidable procedures at such a low level that it is reasonable to recommend these same procedures.

In both instances reported here the entire stomach and a fairly long segment of the lower esophagus should have been removed in order to give the patient the optimum possibility of a cure. The defect so created in the gastrointestinal tract is sufficient to pose a definite technical problem as to the proper method of re-establishing continuity (Fig 8).



We have occasionally encountered a jejunum with sufficient mesenteric length to allow a loop to be drawn up into the chest for several inches. The fact that this can be enhanced by division of the mesentery close to the radix has been shown. However, such a procedure will not always be possible and in fact can be done only rarely. A Roux Y, on the other hand, can be constructed easily. It gives a considerable length of free jejunum. It occurred to us that the defect occasioned in both cases of this type herein reported would have been best repaired by such a procedure. Garlock recently recommended such a procedure.

*Use of the Roux Y in Transthoracic Resections of the Esophagus and Stomach*—In the last few months, we have had occasion to use the Roux Y with satisfaction in two patients who were operated upon transthoracically in whom the entire stomach and the lower end of the esophagus were removed.



Fig. 1. Case 2.—Photograph A, jejunum showing retrocurved size of tumor and the Roux Y tube in place, through which several calculated diets were administered. B, Post-operative film showing junctions between esophagus and jejunum. Not much filling of the jejunum and absence of dilatation in upper esophagus.

CASE 2 (B. & E. N. 11,600 and No. 114,526).—X-ray examination of J. I. revealed no evidence of obstruction at the cardia of the stomach, apparently caused by an underlying malignancy. The lower end of the stomach (Fig. 3, A) is in poor condition, malnourished, and indurated. Fortunately the decompression tube which had been introduced into the esophagus passed through the obstructed area and was able to force food into the stomach. In this tube before the operation. Although he did not gain weight on this regimen, and although we could not bring nitrogen balance studies to a general conclusion obviously improved, judged by appearance, gain in strength, and mental attitude.

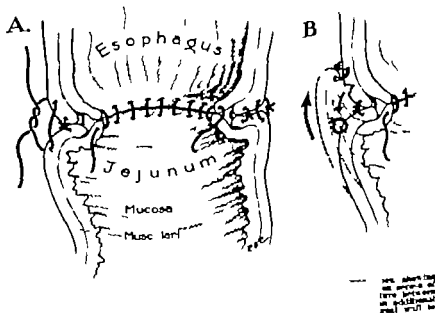
The patient operated post J. I. 30.1.1. The entire stomach and the lower end of esophagus were removed. A Roux Y was constructed and full end esophagojejunostomy was constructed (Fig. 3, B). The newly constructed gut was at first rather as dropped back into the mediastinum and the peritoneal pharynx lined over. The patient soon showed a successful X-ray studies made three months postoperatively showed some



questionable obstruction to the esophagus (Fig 5 B). Although he did develop slight delay in the passage of food down the esophagus, the swallowing mechanism seemed to be functioning properly. A esophagoscopy examination showed no obstruction. A cerebral accident occurred which resulted in his death on Nov. 13, 1947. Autopsy revealed no obstruction of the esophagus to the site of anastomosis. Multiple cerebral infarcts were found, which probably explain the degenerative disability.

CASE 4 (R & P No. 112,654).—P. D. had symptoms very similar to that in Case 3. At the time of operation, the same procedure was carried out except that it was necessary in this case to respect the transverse colon because of direct invasion by the primary tumor. The colon was exteriorized through a small incision in the abdominal wall.

The postoperative course was complicated by the development of a strangulated intestinal obstruction on the third postoperative day. This occurred because a loop of jejunum became doubly strangulated both above the transverse mesocolon and below the diaphragm. This was repaired by one of us (J. P. Y.) and the patient recovered but later he developed—apparently as a result of the pressure—a leak, not at the suture line but in the jejunum, which eventually led to death from sepsis about one month later.



Comment.—In these two cases we found that the construction of a Roux-Y provided us with a very loose segment of bowel which could be anastomosed to the esophagus without tension. The jejunum seems much more adaptable to the anastomosis to the esophagus than does the stomach. The softness and pliability of the jejunum is much more like that of the esophagus, whereas the stomach has a relatively heavy muscular wall. The jejunum offers the additional advantage of distensibility so that an added row of sutures which pulled the loose jejunum more cephalad actually resulted in the jejunum telescoping the lower end of the esophagus so readily and easily that the danger of a leak seemed minimal (Fig 6). In addition to this, we noted that the jejunum corresponded almost



questionable obstruction at the stoma (Fig 5 B). Although he did develop slight delay in the passage of food down the esophagus, the swallowing mechanism seemed to be functioning properly. An esophagoscopic examination showed no obstruction. A cerebral accident occurred which resulted in his death on Nov 12, 1947. Autopsy revealed no obstruction of the esophagus at the site of anastomosis. Multiple cerebral infarcts were found, which perhaps explain the deglutition difficulty.

Case 4 (R & F No. 112 696)—F D had diagnosed erythema that in Case 3. At the time of operation, the same procedure was carried out except that it was necessary at this time to resect the transverse colon because of its involvement by the primary tumor. The colon was exteriorized through stab wound in the abdominal wall.

The postoperative course was complicated by the development of strangulated intestinal obstruction on the third postoperative day. This occurred because loop of jejunum became doubly strangulated both above the transverse mesocolon and below the diaphragm. This was repaired by one of us (J P Y) and the patient recovered, but later he developed apparently as a result of the pressure—a leak, not at the suture line but in the jejunum, which eventually led to death from toxemia about one month later.

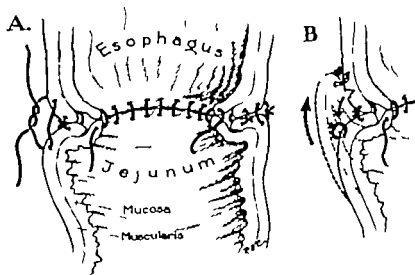


Diagram illustrating the construction of a Roux-Y esophagojejunostomy. The diagram shows the esophagus and jejunum with sutures indicating the anastomosis. The labels 'Esophagus', 'Jejunum', 'Mucosa', and 'Muscularis' are present. An arrow indicates the direction of flow.

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exactly to the size and shape of the resected esophagus, allowing us to replace the site of anastomosis into the already evacuated lower mediastinum (Fig. 1, B). In fact, the facility of this procedure was so great that we felt that it would be much more likely to be well tolerated than would the more standard operation of anastomosis between the remaining fundus of the stomach and the lower end of the esophagus. In the more customary procedure the stomach is left occupying space within the chest which would otherwise be occupied by the lung (Fig. A) whereas the use of the Roux Y allows the site of the anastomosis to drop back into the mediastinum permitting full expansion of the lung. This makes postoperative ventilation and care much simpler.

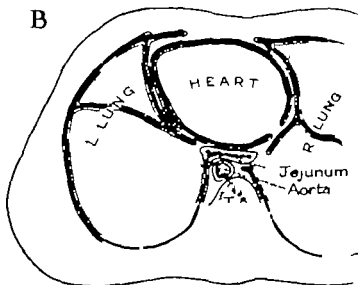
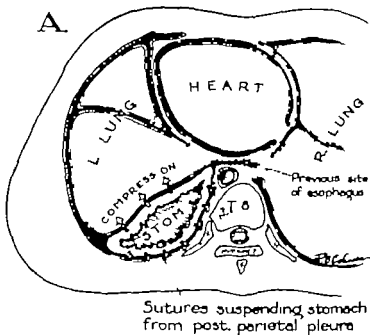
*Use in High Esophageal Anastomoses*.—Encouraged by the facility of this operation and by the report of Rienhoff and Garlock, we extended this approach to cure for the reconstruction of the esophageal defect in one patient with a high lying carcinoma of the esophagus. Because of the tremendous length of jejunum needed, we elected the Rienhoff procedure of construction of the Roux Y at a preliminary abdominal operation, to be followed in a few days by the definitive resection of the tumor and anastomosis between the esophagus and jejunum.

(Case 3 (R. & E. No. 11450).—G. L. had no evidence of carcinoma in the middle third of the esophagus as operated upon Nov. 26, 1941 transabdominally. A large blind segment of jejunum constructed in this case dividing the celiac arteries close to their origin to the superior mesenteric artery as possible. This was obviously done to preserve the side branches to the bowel. Before each anastomosis as severed, bulldog clamps are applied to determine the extent of the collateral circulation. At the time of completion of this 30 in. loop the bowel was pink and shiny and definite pulsation could be seen in the arteries. The jejunum had been divided only 1 cm distal to the ligament of Treitz (Fig. 2). After sixteen hours the patient rather rapidly developed evidence of severe abdominal pain and exploration revealed that the entire blind loop which we had constructed had become gangrenous and had to be resected. Subsequent gastrostomy was resorted to, but the patient died later of inanition.

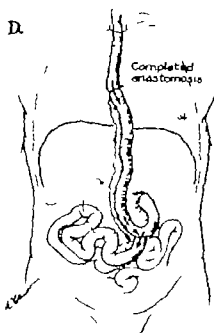
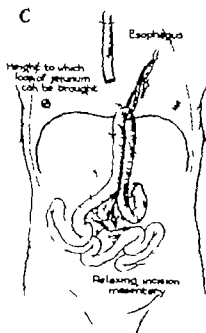
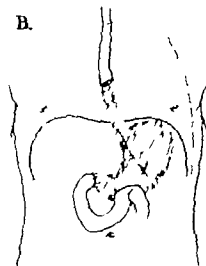
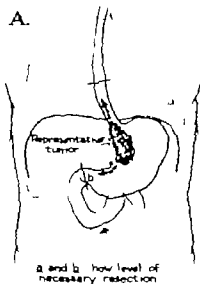
Analysis of this patient seemed for the period immediately following the construction of the Roux Y made feel that in this case retrograde venous thrombosis had precipitated the gangrenous process in the bowel, since at the time of closure of the abdomen the arterial system was adequate. It appears that the construction of this very long branch might well be staged so that at the first operation of the long segment of bowel might be freed from its attachment close to the superior mesenteric artery but left intact. When the definitive resection could be carried out several days later this loop of bowel could have had time to develop collateral and could then be of useful length. In addition, this, if led to take Rienhoff's detailed recommendation that anastomosis

(Fig. 1)

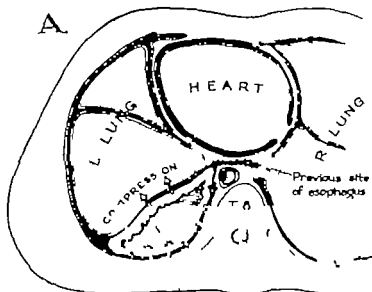
Provision was made for the first branch of the superior mesenteric artery of the great importance in maintaining deep-seated circulation to the mobilized loop of the jejunum. This first branch is the largest of all the celiac vessels jejunally. It is almost as large as the descending aorta. To obtain the largest derived from the primary from its root, division or transection of the jejunum is performed 10 to 20 cm from Treitz ligament. All previous operations have divided the jejunum close to its origin, least 6 to 9 cm beyond Treitz ligament. When the intestine is mobilized each anastomosis the blood supply to the small intestine is the primary dependent upon the blood supply to the small intestine from the smaller more distal branches of the superior mesenteric artery which are the fifth and sixth branches. After division of the jejunum 20 to 40 cm from



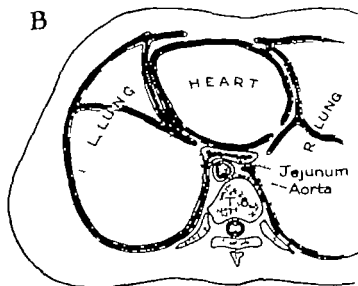
traction of the  
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is -- illustration of the mechanical problem involved in the entire approach and rather he does not see of making the statement -- he from individual much power. I believe high I am understood in the



Sutures suspending stomach  
from post. parietal pleura



Portion of the  
left lung resected  
to avoid the  
aorta





Treitz's ligament the oral end of the proximal loop is then brought into the chest instead of the buccal end of the distal loop. Perri's law does not interfere with the satisfactory function of this loop.

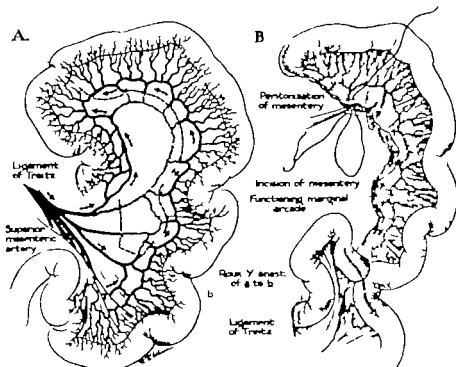


Fig. 8.—Chemical Loop. A represents the first portion of jejunum with blood supply from the superior mesenteric artery. Dotted box indicates segment of bowel to be included in Roux Y. Note the blood supply to this segment must come from short renal supplied by small jejunal branches. B illustrates Roux Y practically completed.

*Use in Abdominal Gastrectomies*—We felt that with the Roux Y technique there would be little if any danger of duodenal stump blow out. Our thought in this regard was encouraged by the recent work of Orr, who, in March, 1947 reported his experience with the use of the Roux Y in abdominal gastric resection. We had had one such patient in the past, in whom a kink between the ligament of Treitz and the esophageal anastomosis had resulted in extensive gangrene of the duodenum with resultant necrosis of the entire segment.

CASE 6 (Pt. L. K. 54018).—M. L. was entered Pe Lab. Hospital on June 18, 1944. A transverse gastrectomy for obvious carcinoma was done on June 21, 1944. The first two postoperative days were complicated by massive pulmonary atelectasis. The mucus was easily coughed out. On the morning of the third day, tender palpable mass was felt in the abdomen and the pulse was noted to be 120 for the first time. A diagnosis was difficult to make and since thought it might be hematoma from an unrecognized bleed it was decided that the patient should be operated upon. The hematoma of 49 led us to administer 800 cc. plasma preoperatively. Laparotomy revealed the presence of a kink in the proximal loop of the jejunum between the ligament of Treitz and the anastomosis. This was easily freed and allowed the accumulated content with the duodenum to pass distally beyond the stomach and into the jejunum. It had been noted that the duodenum was considerably dilated before this kink was released, but following the release the color of the duodenum returned and we felt that the wall of the duodenum was viable.

sions (pulmonary atelectasis, pleural effusion, mediastinal shifts, possible leak at site of anastomosis, etc.) This makes it imperative that we achieve optimal preoperative conditions.

Such patients must receive especial attention to their nutrition. High vitamin, antianemic diets, containing 900 Gm. of protein per day are advised for a period of two weeks if possible. The case of Mr J I mentioned previously should be noted. In that case the decompression tube which unexpectedly passed through the previously obstructed cardia of the stomach allowed us to give him a relatively normal alimentation for sixteen days. This not only spared the veins, but definitely improved the ability to withstand the operation.

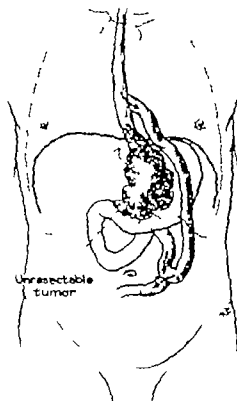


FIG. 1.—This is to illustrate the size of the tumor, its location, and its position in the stomach. The tumor is located in the pyloric region of the stomach. The tumor is large and irregular, and it is shown to be unresectable.

The addition of large amounts of the essential vitamins should be attended to. 500 mg. of vitamin B<sub>1</sub>, 100 mg. of vitamin B<sub>2</sub>, and twice the daily requirement of the B complex should be administered either orally or parenterally.

We feel that preoperative gastrotomy is amply indicated and prefer to proceed with the resection as soon as possible.

The patient's fluid requirements on the operating table should be anticipated by the placing of a cannula within the vein. We elect to avoid a needle insertion in the femoral vein because displacement toward the end of the procedure when fluid and/or blood is of paramount importance. It will be difficult to replace. In addition to this, in one patient we had inadvertently resected a small portion

We have utilized the Roux Y procedure in three abdominal total gastrectomies with satisfaction. In all of these both the technical execution of the operation and the recovery of the patient have been satisfactory.

*Palliation.*—The facility with which the loop of Roux Y can be manipulated has allowed us recently to utilize this procedure in one case as a means of restoring deglutition to a patient whose carcinoma could not be removed.



Fig. 11. Case of the stomach. T<sub>1</sub> taken on the seventh day, into the side of as readily as down.

CASE 7 (R. & E. N. 115,303).—G. W. entered the hospital Dec. 20, 1917 with diagnosis of carcinoma of the stomach (Fig. 11). A transverse exploration, carried out the abdomen revealed the presence of an enormous carcinoma which not only replaced most of the stomach, but which had invaded through the pancreas and at the retroperitoneal tissues to such an extent that even resection of the stomach with the pancreas and transverse colon would have been impossible. The bulk of the tumor was very great, being fully 10 by 10 by 10 cm. A Roux Y was constructed whose length was easily made suitable to pass around the tumor through the diaphragm and up to level at which it could be anastomosed to the side of the esophagus (Fig. 12). The postoperative course was smooth. H. was able to eat liberal soft diet on the seventh postoperative day (Fig. 11 B). Eushed and similar procedure for case of achylia with gratifying result.

DISCUSSION

—case the nutritional problem they must undergo a long danger of many complications.

The actual anastomosis itself (Fig 14) we have attempted to accomplish in such a way that there is a considerable breadth of contact between the wall of the esophagus and the wall of the jejunum. We have found that interrupted white cotton or silk sutures may well establish an outer sero-serous layer. These sutures should all be placed before being tied, as shown in Fig 13 B to avoid inadvertent tearing of the delicate esophageal wall. Following this the

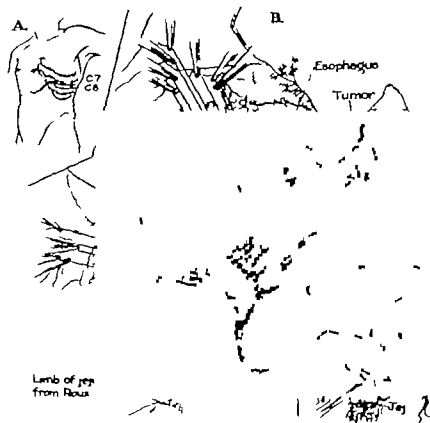


FIG. 13.—A and B. (A) shows the esophagus and jejunum. (B) shows the esophagus and tumor. (C) shows the limb of the jejunum from the flow.

esophageal musculature is needed at least 1 inch away from the layer of sutures. Because of the thickness and separateness of the esophageal musculature we have sutured the cut end of the esophageal musculature to the serosa of the jejunum as second layer in our anastomosis. This has been done with interrupted fine black silk (Fig 14 B). The mucosa of the esophagus is opened and a continuous suture of very fine (00000) chromic catgut suture is used to join proximal these structures (Fig 14 C and D). The middle and exterior row of sutures are then placed on the interior portion of the anastomosis (Fig 14 E and F). At the completion of the anastomosis no black silk sutures should

of the vena cava in resecting the tumor-bearing lymph nodes about the hilus of the stomach. The ease with which the temporary but severe blood loss was replaced through our open cannula more than justified the time required to place it at the beginning of the operation. Whole blood administered at a rate of 1 liter an hour had been found to be optimum in covering the sensed and unsensed blood loss. This, of course may be increased at the discretion of either the surgeon or the anesthesiologist.

**Incision.**—The combined abdominothoracic incision of the type recommended by Carter and associates, Humphries, and Gluck<sup>2</sup> is the incision of choice in such cases. Such an incision allows abdominal exploration to determine resectability of the tumor. It allows adequate exposure for careful assay of the extent of the lesion and more expedient execution of the operation. Perhaps more important than anything else the esophageal anastomosis which must be done with meticulous care can be executed in the center of the perath field, where it is the easiest to do (Fig. 13). The fact that we have done gastrectomy through a simple abdominal approach with success does not lessen the greater value and safety afforded by the combined incision. In one recent case, a tear in the wall of the esophagus was made entirely made in placing a serosal suture. This tear resulted not so much from carelessness in placing the suture (because we were being very careful) as from the fact that the tension which was placed upon the esophagus to hold it down into the abdomen (to a level at which we could operate) was so great that the esophageal wall had been unexpectedly (and inexcusably) thinned out. The defect was luckily recognized and covered (Fig. 6). This hazard would not have been necessary had the proper incision been employed.

**Resection.**—In addition to the necessity of resecting all of the tumor-bearing portions of the esophagus and stomach, the neighboring lymph node-containing tissues must be resected. This means that the entire gastrophrenic omentum with its lymph nodes and the great omentum must be removed. The resection of neighboring organs which are involved by direct extension of tumor is also indicated. Thus the colon spleen, pancreas, left lobe of the liver and sometimes even the left kidney may be removed en bloc with the specimen.

**Anastomosis.**—In attempting to prevent leakage from developing at the anastomotic line we feel that there are two factors of importance. First is the provision of the loop of Roux-Y which is completely free from tension. Second is the detailed care used in establishing the anastomosis. The laxness and freedom from tension desired in the Roux-Y can be assured by the adequate freeing of the mesentery of the jejunum and can be maintained after anastomosis by the use of relaxing stitches which hold the jejunum up toward the esophagus. These stitches can be placed between the parietal pleura and the jejunum or between the jejunum and the loose connective tissue in front of the vertebrae. These fixation sutures should be placed at several levels, not only thoracically but actually abdominally to help immobilize the segment of jejunum in place above the transverse mesocolon. We prefer to bring this loop of jejunum through the transverse mesocolon since it shortens the length of bowel necessary and since actually it places the jejunum in the right direction to enter the esophageal hiatus of the diaphragm without kinking.

A tube for decompression has been used in all of these cases, 1 ft down to a level just above the esophagejejunal anastomosis. It has been both surprising and gratifying to find that jejunal contents were aspirated through the Levine tube on the third day in several cases, thus indicating the absence of stomal closure by postoperative edema.

Closure.—The detail of closure must be executed with care. In one case noted here strangulation occurred as a result of inadequate closure of the transverse mesocolon and diaphragm. In addition accurate and secure closure of the thoracic cage is necessary to restore its strength. The patient must be able to cough freely and vigorously postoperatively. Pericostal sutures and secure closure of the musculature of the abdominal and thoracic wall should be made. The importance of expectorating mucus plugs in cases of this nature is well known to all. In our series, not mentioned herein, and not done for carcinoma of the cardia failed to provide a secure chest wall resulted in fatal pneumonia.

#### CONCLUSIONS

1 The utilization of the Roux-Y partially makes more radical resection possible in cases with carcinoma centered about the cardia of the stomach.

2 We believe that this technique usually lowers the operative mortality and it allows more complete resection of the tumor and particularly because it allows easier technical execution of the anastomosis.

3 It should be a method with very little danger of duodenal stump blowout.

4 The jejunum placed in the thorax occupies only the space in the mediastinum created by the removal of the esophagus. This avoids the compression of the lung which occurs in some extent when the stomach is brought up into the chest and thus compresses the esophagus.

5 Its use in isolated cases as a means of palliation is suggested.

6 Some important technical detail is emphasized.

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2. (2) *Arch. J. H. Coll. and Abdom. and Thorac. Approach of Carcinoma of the Cardia of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
3. (3) *Arch. J. H. Coll. and Abdom. and Thorac. Approach of Carcinoma of the Cardia of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
4. (4) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
5. (5) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
6. (6) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
7. (7) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
8. (8) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
9. (9) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.
10. (10) *Esophagectomy for Lesions of the Upper End of the Stomach and Lower End of the Esophagus*. *Proc. B. Vol. 11, no. 31/32*, p. 272.

be visible between the white silk sutures used in the outer layer. As mentioned previously, the pliability of the jejunum allows it to be drawn up around the esophagus as a cuff and this can be extended when any technical error has caused a tear in the esophageal wall.

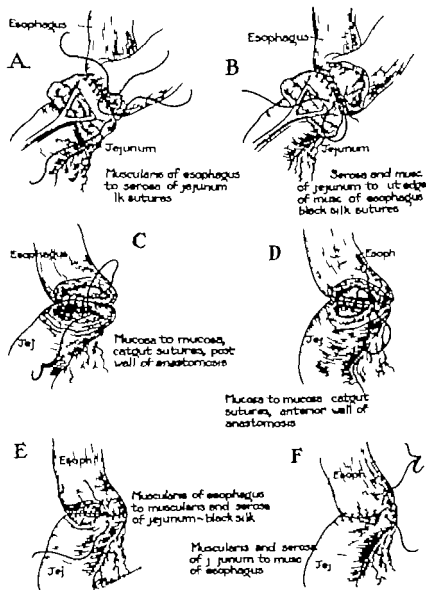


Fig. 14.—Technical details of an esophagojejunostomy. A. A study placed in interrupted sutures are shown being tied. B. The serosa and mucosa of jejunum should be drawn up to the edge of the mucosa of the esophagus. This is to allow for the anastomotic constriction which allows fusion. C and D show the use of catgut for the mucosa-to-mucosa sutures. E. The middle row of interrupted sutures. Black silk is used so it can be seen and excluded by the last layer illustrated in F.

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**Closure.**—The details of closure must be executed with care. In one case cited here strangulation occurred as a result of inadequate closure of the transverse mesocolon and diaphragm. In addition accurate and secure closure of the thoracic cage is necessary to test its strength. The patient must be able to cough freely and vigorously postoperatively. Pericostal sutures and secure closure of the musculature of the abdominal and thoracic wall should be made. The importance of expectorating mucous plugs in cases of this nature is well known to all. In one of our cases, not mentioned herein and not done for carcinoma of the cardia failure to provide a secure chest wall resulted in fatality from unexpected mucous.

# CONCLUSION

1. The utilization of the Roux-Y procedure makes more radical resections possible in cases with carcinoma centered about the cardia of the stomach.

We believe that this technique may actually lower the operative mortality since it allows more complete resection of the tumor and particularly because it allows easier technical execution of the anastomosis.

3. It should be associated with very little danger of duodenal stump blowout.

4. The jejunum placed in the thorax occupies only the space in the mediastinum created by the removal of the esophagus. Thus avoid the compression of the lung which occurs to some extent when the stomach is brought up into the chest and anastomosed to the esophagus.

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# INTRAHEPATIC CHOLANGIOJEJUNOSTOMY WITH PARTIAL HEPATECTOMY FOR BILIARY OBSTRUCTION

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## INTRODUCTION

THIS report presents a method of treating extensive obstructions of the common duct or common hepatic duct by anastomosing one of the intrahepatic biliary ducts to the jejunum following partial resection of the left lobe of the liver. The procedure has been successfully employed in one case of recurrent obstruction of the common hepatic duct and attempted unsuccessfully in three cases of congenital biliary atresia in which previous explorations had shown complete absence of the extrahepatic biliary system.

Restoration of the function of the sphincter of Oddi is desirable in choledochostomy and as has been stressed by Lahey, Cattell and others whenever possible the continuity of the biliary tract should be re-established by some type of anastomosis of the duct above and below the point of obstruction. Unfortunately such a procedure is at times not feasible and some type of choledochointerostomy or cholecystenterostomy must be substituted. It is only in those cases where all such methods have proved inadequate that an attempt may be made to utilize an intrahepatic duct for biliary drainage.

**Technique.**—The abdominal incision is entered through a V-shaped bilateral subcostal incision which is extended further to the left than to the right. Any adhesions about the left lobe of the liver are freed. The triangular ligament is divided and the left lobe of the liver is elevated from the diaphragm (Fig. 1). A piece of wide tape is passed about the base of the left lobe and traction is applied to hold this portion of the liver firm. Starting at the anterior edge of the left lobe just to the left of the round ligament two or three mattress sutures of large sized catgut or heavy silk are placed through the entire thickness of the liver and the left lobe is partially divided just distal to these sutures, thus bringing the liver vessels into the middle third of the left lobe. While the liver substance is compressed between the thumb and index finger to control bleeding the incision is extended just medial to the careful inspection of the proximal cut surface for evidence of major bile duct. If no such duct is encountered after extending the incision for about 1½ cm an additional mattress suture is placed through the liver and the incision continued until a duct of suitable caliber is identified. Releasing the compression and allowing blood to escape from the cut surface will aid in differentiating veins from ducts, although before the anastomosis is begun a catheter is inserted into the duct and bile is aspirated for positive identification. Bleeding from the liver above and below the selected duct is somewhat more difficult to

control but may be treated by the application of some hemostatic agent such as Gelfoam or by carefully placed sutures which include the tissue above and below the duct.

After a suitable duct is identified the liver incision is extended to the nearest point on the edge of the lobe. A wedge-shaped segment of the left lobe is resected and hemorrhage again controlled with through-and-through mattress sutures. The liver tissue immediately surrounding the selected duct is then scored out with a scalpel or curette to give additional length of the duct for the reconstruction. In cases of biliary obstruction in adults the major intrahepatic duct are dilated and have thickened fibrosed walls which are well suited for a suture anastomosis (Fig. 3).

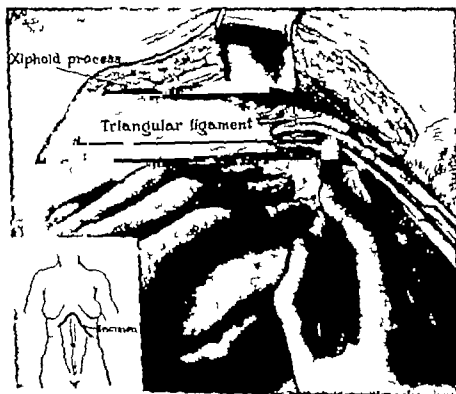


Fig. 1—Dissection of left hepatic lobe by division of triangular ligament. All total abdominal incision shown in figure.

A suitable loop of jejunum is selected for the anastomosis and a suture for interrupted sutures is placed between the inferior portion of the cut liver capsule and the mesenteric border of the intestine (Fig. 4). A small opening then is made into the lumen of the jejunum opposite the selected duct and the liver wall is sutured to the mucosa and submucosa with interrupted sutures (Fig. 5). A short segment of rubber catheter is cut and with catgut suture is

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— (Fig 1)

action is  
erect edge

of the left lobe just to the left of the round ligament. Two mattress sutures of large sized catgut or heavy silk are placed through the entire thickness of the liver and the left lobe is partially divided just distal to these sutures, thus bringing the biliary network to the middle third of the left lobe. While the lobe is suspended it is compressed between the thumb and index finger. With control bleeding the incision is cautiously extended posteriorly with careful inspection of the proximal cut surface for evidence of a major bile duct (Fig 2). If no such duct is encountered after extension of the incision for about 1½ in. an additional mattress suture is placed through the liver and the incision continued until a duct of suitable caliber is identified. Releasing the compression and allowing blood to escape from the cut surface will aid in differentiating veins from ducts, although before the anastomosis is begun a catheter is inserted into the duct and bile is aspirated for positive identification. Bleeding from the liver above and below the selected duct is somewhat more difficult to



Fig. 1—Antimesenteric border of jejunal loop is sutured to inferior cut edge of liver. A small incision is made in jejunal wall for the anastomosis. Small above: cross section of completed anastomosis. The antimesenteric border of jejunal loop and red is superior surface of liver.



Fig. 2—End of intrahepatic duct is sutured to side of jejunal loop. Interohepatic duct is interrupted either by

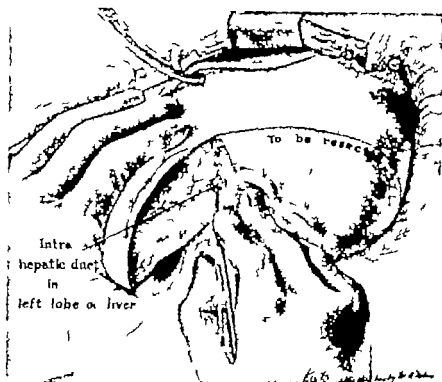


Fig. 1—Dissection of liver to reveal intrahepatic duct. Identification of intrahepatic duct.



Fig. 2—Cut surface of left lobe of liver after edge resection. Matzen suture directly on intrahepatic duct does not pass completely through liver. It includes only the tissue above duct. A similar suture placed on the undersurface of liver includes it or tissue inferior to duct.

The results of laboratory tests were follows: Serum bilirubin, total, 12.0 mg per cent direct, 10.0 mg per cent; phosphatase, 14.4 units; total serum protein, 7.5 Gm. per cent; albumin, 3.9 Gm. per cent; globulin, 4 Gm. per cent; thyroid turbidity 7.4; prothrombin time 39 sec. 63 per cent of normal.

The result to be that had been placed through the bile duct just posterior to the previous operation was now seen by x-ray examination of the abdomen to have passed into the left lower quadrant.

With a preoperative diagnosis of recurrent complete biliary obstruction, an exploratory laparotomy was performed April 1, 1941. The neck of the operation has been outlined in the preceding section. A transhepatic duct which admitted a size 14 French catheter was used for the anastomosis. The intrahepatic duct contained what bile with occasional strands of green stained mucoid material. A very short jejunal loop as satisfactorily used and it not feasible to perform the enterocystostomy as recommended.

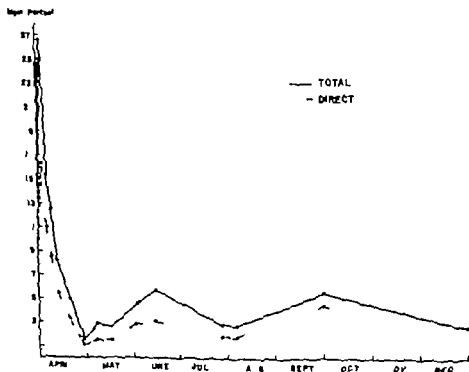


Chart 1—Serum Bilirubin levels of patient before and after intrahepatic cholelitholectomy (Operation performed April 2, 1941)

Postoperative ileus was noted in the small for the first time on the seventh day and was present a full 24 hours after operation. The temperature was 101° during the first 10 and one-half weeks after operation, but declined after definite determination of the cause. The fever was in part accounted for by the daily intravenous injection of protease hydrolytic solution as it subsided shortly after these injections were stopped. The short jejunal loop with angulation at the ligament of Treitz was responsible for the occasional attacks of vomiting which occurred during the first three weeks after operation. A small quantity of bile stained stool escaped from the peritoneal cavity below the drain during the first six days after operation. There was no subsequent drainage. The wound healed per primam. Microscopic sections of the liver tissue removed at operation showed evidence of biliary obstruction.

such a way that it passes through the anastomosis into the bile duct. The antimesenteric border of the jejunum is sutured to the superior surface of the liver capsule along the cut edge. This maneuver completely peritonealizes the entire raw liver surface and re-enters the anastomosis. An enteroenterostomy should be performed between the two jejunal loops proximal to the biliary anastomosis (Fig 6). If desired, a Roux type segment of the jejunum as described by Allen may be used for the anastomosis. The region of the anastomosis is drained and the incision closed in layers.

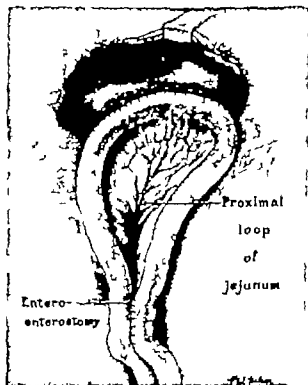


FIG 6.—Completed anastomosis with enteroenterostomy between two limbs of jejunal loop.

#### CASE REPORT

M. W., a 64-year-old colored woman, was admitted to the hospital with signs and symptoms of complete biliary obstruction. Two previous attempts had been made to correct an acquired stricture of the common duct. At the first operation on Sept. 16, 1943, an end-to-end repair of the duct was performed. At the second operation on Nov. 23, 1944, a very short segment of the proximal end of the common hepatic duct was anastomosed to the jejunum. Both procedures had been temporarily successful but obstructive signs had returned after a few months. The patient was known to have been jaundiced for at least three months prior to the present admission. On physical examination there was evidence of weight loss and marked jaundice. The stools were completely acholic. The urine was highly colored and gave positive test for bile.

The result of laboratory tests were as follows: Serum bilirubin, total, 23.6 mg per cent direct, 10.0 mg per cent phosphatase activity 5.1 units total serum proteins, 7.4 Gm per cent albumin, 3.0 Gm per cent globulin, 2.4 Gm per cent thyroglobulin 1.4 prothrombin time 19 sec 65 per cent of normal.

The rubber tube that had been placed through the hepatocholejojunostomy at the previous operation was now seen by x-ray examination of the abdomen to have passed into the left lower quadrant.

With preoperative diagnosis of present complete biliary obstruction, an exploratory laparotomy was performed April 2, 1947. The technique of the operation has been outlined in the preceding section. An intrahepatic duct which admitted a size 14 French catheter was used for the anastomosis. The intrahepatic duct contained a bit bile with occasional strands of green stained mucoid material. A very tight jejunal loop was anastomosed and it was not feasible to perform the extrahepatic anastomosis recommended.

Figure 1

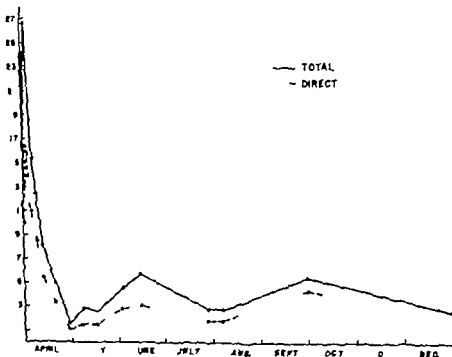


Chart 1—Serum bilirubin levels of patient before and after intrahepatic cholangiojejunostomy. Operation performed April 2, 1947.

Postoperatively bile was noted in the stool for the first time on the seventh day and was present in specimens after that time. The temperature was elevated during the first two and one-half weeks after operation, but declined about definite determination of the cause. The fever was in part accounted for by the daily intravenous injection of protein hydrolyzate solution. It subsided shortly after these injections were stopped. The short jejunal loop, its angulation at the ligament of Treitz or responsible for the occasional attacks of vomiting which occurred during the first three weeks after operation. A small quantity of bile-stained fluid escaped from the peritoneal cavity about the drain during the first 24 days after operation. There was no subpyloric drainage. The incision healed per primam. Microscopic sections of the liver tissue removed at operation showed evidence of biliary cirrhosis.



After an initial rise the blood bilirubin fell, and although it remained at a slightly elevated level there were clinical symptoms of jaundice for only two brief periods when the serum bilirubin was elevated to 5.5 mg per cent (Chart 1). On both occasions the only symptom was mild generalized itching. Bile was always present in the numerous stool specimens examined. Appetite remained good. Upon questioning, the patient professed to have vague intermittent abdominal discomfort which, however, was never severe enough to prompt her return to the outpatient clinic except when asked to return for follow-up studies. On the last visit, nine months after operation, the patient's general condition was good. She was eating well. There had been slight gain in weight and she seemed definitely stronger. The sclera were normal color. There was slight icterus of the oral mucous membranes. A specimen of stool contained bile. Fom test of the urine was negative for bile. The following laboratory tests were obtained: Nephrotoxin antigen, 23 mg. per cent; blood sugar 84 mg per cent serum bilirubin, total, 7 mg per cent, direct, 1.8 per cent refractive index, 1.014 per cent protein; cephalin flocculation, negative; thymol turbidity 5.6 units.

The procedure was unsuccessfully attempted on three infants who had been found at a previous operation to have complete agenesis of the extrahepatic biliary system. In the first of these it was thought at operation that a very small intrahepatic bile duct had been cannulated with a ureteral catheter and implanted into the jejunum. The stools were a green color for about three days after operation then they again became acholic and remained so. At re-exploration three weeks later the mucosa of the jejunum was found to be healed over in the region of the anastomosis, and there was a cyst containing about 1 cc of bile-stained fluid between the mucosa of the bowel and the surface of the liver. The cyst wall was opened widely into the lumen of the jejunum and again green colored stools were passed for a period of four days after operation before they became acholic. The child subsequently died and at post mortem examination the cyst was found to be no communication between the jejunum and the intrahepatic biliary system.

In the second case we were unable to locate any suggestion of an intrahepatic duct and microscopic sections of the liver tissue removed showed bile canaliculi but no bile ducts. It was our conclusion that this child had agenesis of both the extrahepatic and intrahepatic biliary systems.

In the third patient a fibrous cord 3 to 4 mm in diameter was found in the mid portion of the left lobe of the liver. This cord contained two relatively large veins, an artery and, in addition, at least three minute openings could be seen from which small amounts of bile-stained fluid could be expressed. The vessels were individually ligated and the stalk was implanted into the lumen of the jejunum. Green stools were passed for seven days postoperative. They then became acholic and remained so until the child died on the twelfth day after operation. At autopsy the region of the anastomosis was seen to be well healed. The fibrous cord could be seen projecting into the lumen of the jejunum but there was no opening into the biliary system.

It was felt that in two of these cases we had been able to establish a temporary biliary intestinal communication but we have been unable to devise a method of keeping this small opening patent.

## DISCUSSION

Although the indications for the procedure herein described are quite limited, the technique does offer a rational surgical procedure for a certain group of cases of biliary obstruction in adults, the treatment of which has hitherto been unsatisfactory. When the procedure is indicated it has certain very definite advantages over the usual orthodox approach. Instead of re-entering the previous operative field about the hilus of the liver and the hepatoduodenal ligament where dense vascular adhesions and obliteration of landmark make dissection extremely tedious and hazardous, an approach through the left upper quadrant avoids most of the scarring and adhesion from previous irritation. A minimal amount of adhesions is encountered to the left of the ligamentum teres even in patients who like the one reported, have undergone several previous operative procedures.

With the left lobe of the liver elevated in the manner described the exposure and accessibility of the selected intrahepatic duct are such that a much more accurate anastomosis can be performed between the duct and the intestine than is frequently possible when attempting to use a short stump of the common hepatic duct deep in the hilus of the liver. Ladd and Gross, Walters, and Heim, Cole and associates, and others have stressed the importance of accurate approximation of the mucosa of the duct and the intestine to prevent subsequent strictures and associated cholangitis.

Several anatomic changes occur in the chronically obstructed liver which make the organ more amenable to surgery than the normal liver. The generalized increased fibrosis associated with the biliary cirrhosis and the thickening of Glisson's capsule allow mattress sutures through the liver substance to be tied accurately without cutting through the tissue. The periductal fibrosis thickens the duct wall so that it is well adapted to a suture anastomosis, and the generalized dilatation of the duct system provides a larger intrahepatic opening into the biliary tree than would normally be available.

If the extrahepatic obstruction is high enough to block the communication of the left and right main hepatic ducts, a condition which probably occurs very infrequently, it is uncertain how much of the liver substance would be drained by the procedure. Little is known about the communication of intrahepatic bile channels in the presence of obstruction of a portion of the biliary tree in man. Experimental studies have shown considerable variation in the reactions of different laboratory animals to obstruction of a portion of the biliary system.

Levant, Cantarow, and Morgan found no evidence of intrahepatic biliary communication between the obstructed and nonobstructed portions of the cat liver. They noted a sharp line of demarcation between the two liver segments. Demonstrable impairment of hepatic function occurred occasionally following the ligation of a single extrahepatic duct. Harley and Barratt found little gross difference between the obstructed and nonobstructed segments of the cat's liver after five to six months. Rous and Larimore<sup>8</sup> observed a rapid atrophy of the obstructed portion of the rabbit liver with commensurate hypertrophy of the unobstructed segment, the former being reduced to a fibrous tag at the

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It was felt that in two of these cases we had been able to establish a temporary biliary intestinal communication, but we have been unable to derive a method of keeping this small opening patent.

# DISCUSSION

Although the indications for the procedure herein described are quite limited, the technique does offer a rational surgical procedure for a certain group of cases of biliary obstruction in adults, the treatment of which has hitherto been unsatisfactory. When the procedure is indicated it has certain very definite advantages over the usual orthodox approach. Instead of re-entering the previous operative field about the hilus of the liver and the hepatoduodenal ligament, here dense vascular adhesions and obliteration of landmarks make dissection extremely tedious and hazardous, an approach through the left upper quadrant avoids most of the scarring and adhesions from previous operation. A minimal amount of such reaction is encountered to the left of the ligamentum teres even in patients who like the one reported have undergone several previous operative procedures.

With the left lobe of the liver elevated in the manner described, the exposure and accessibility of the selected intrahepatic duct are such that a much more accurate anastomosis can be performed between the duct and the intestine than is frequently possible when attempting to use a short stump of the common hepatic duct deep in the hilus of the liver. Ladd and Gross, Walters, and Heum, Cole and associates, and others have stressed the importance of accurate approximation of the mucosa of the duct and the intestine to prevent subsequent strictures and associated cholangitis.

Several anatomical changes occur in the chronically obstructed liver which make the organ more amenable to surgery than the normal liver. The generalized increased flow associated with the biliary cirrhosis and the thickening of Gibson's capsule allow mattress sutures through the liver substance to be placed securely without cutting through the tissue. The periductal fibrosis thickens the duct wall so that it is well adapted to a suture anastomosis, and the generalized dilatation of the duct system provides a larger intrahepatic opening into the biliary tree than would normally be available.

If the extrahepatic obstruction is high enough to block the communication of the left and right main hepatic ducts, a condition which probably occurs very infrequently, it is uncertain how much of the liver substance would be drained by this procedure. Little is known about the communication of intrahepatic bile channels in the presence of obstruction of a portion of the biliary tree in man. Experimentally, however, as shown considerable variation in the reactions of different laboratory animals to obstruction of a portion of the biliary system. Stewart (Cantow and Morgan) found no evidence of intrahepatic biliary communication between the obstructed and nonobstructed portions of the cat liver. They noted a sharp line of demarcation between the two liver segments demonstrable impairment of hepatic function occurred occasionally following the ligation of a single extrahepatic duct. Harle and Barratt found little gross difference between the obstructed and nonobstructed segments of the cat liver after five to six months. Ross and Larimore observed a rapid atrophy of the obstructed portion of the rabbit liver with a compensatory hypertrophy of the unobstructed segment if the liver being reduced to a fibrous tag at the



Fig. 1.—Rennigram of liver prepared by Sims. Left main hepatic duct filled. Its radiopaque solution left hepatic duct drains left lateral quadrate lobe and major portion of caudate lobe.

Fig. 2.—Rennigram of liver prepared by Sims. Right main hepatic duct filled. Its radiopaque solution right hepatic duct drains the right lobe and major portion of the caudate lobe.

end of four months. These animals remained in good condition and showed no signs of jaundice. Some evidence of intrahepatic biliary communication between the segments was noted.

Study was done on the portions of the liver drained by the right and left main hepatic ducts by tying off one or the other of these ducts, in human livers obtained at autopsy, injecting a radiopaque solution into the remaining patent duct and making a roentgenogram of such preparations. By this method it can be seen that the left main hepatic duct drains the left lobe, the quadrate lobe and most of the caudate lobe (Fig 7). The right main hepatic duct drains the right lobe and a small portion of the caudate lobe (Fig 8). There is no evidence in these preparations of intrahepatic communication of the two duct systems.



Fig 9—Roentgen cast of intrahepatic biliary system after ligation of right and left duct systems.

Injection of the right and left duct system with different colored plastic solution and digestion of the liver substance prepares a cast of the intrahepatic duct system which again emphasizes the rather large portion of the liver drained by the left main duct (Fig 9). There is also evidence that the region of the caudate lobe drained by both the left and right main ducts, and there is suggestion also that the two systems communicate through numerous fine ducts in this area as certain of these ducts contained plastic material of both colors. These observations together with the large functional reserve of the liver would suggest that even in cases where biliary drainage is incomplete it would probably be adequate.

The difficulties encountered in maintaining the patency of the intrahepatic jejunal communication in infant might well make one skeptical of all such anastomoses. In adults, however, we believe it should be possible to obtain

Dr. Robert Phelan, Assistant Resident in the Department of Radiology, The Johns Hopkins Hospital.  
Fluoroscopic technique: 5 per cent solution of meconium.



FIG. 10.—Dog. Liver and tracked fistulae with probe passing through intrahepatic cholangiojejunostomy. The common duct had been ligated and the gall bladder removed prior to the performance of the anastomosis. There is moderate dilatation of the extrahepatic biliary system.



FIG. 11.—Photomicrograph of intrahepatic cholangiojejunostomy showing mucosa-to-mucosa healing.

an intrahepatic luet large enough so that a direct end-to-side anastomosis may be performed and the chances of maintaining the patency of such an anastomosis are much better than in the implantation procedures used in infant. The intrahepatic jejunal anastomosis will of course be subject to all of the complications, such as atresia, ascending infection, and so forth, that occur in anastomoses between the extrahepatic biliary system and the alimentary tract. Certain features of the procedure have been mentioned which might lessen the incidence of such complication when an intrahepatic duct is used.

The procedure has been carried out in dogs to study the performance of the anastomosis and its effect on the liver and remaining luet system. In the animal from which specimens were obtained for Figs. 10 and 11 the common duct was doubly ligated and divided and the gall bladder removed. One week later the major portion of an anterior lobe of the liver was excised and the proximal end of the principal duct anastomosed to the side of a jejunal loop. An enteroenterostomy was performed between the two limbs of the jejunal loop. Two months later at the time the animal was killed, it was in good health, there was no jaundice, and the stools were of normal color. The anastomosis between the bile duct and the jejunum was patent and well healed without evidence of stricture. There was moderate dilatation of the extrahepatic biliary system. The mucosa of the jejunal loop was covered with bile-colored fluid. The duct used in this experiment was considerably smaller than that found in the adult patient previously described. Such experimental results support our view that intrahepatic bile luet may be used for biliary drainage. Further experimental studies are in progress.

Previous rather crude attempts have been made to divert the contents of the intrahepatic biliary system directly into the alimentary tract by resecting a small portion of the free liver edge or by inserting a cautery or a probe into the liver substance and then diverting the resultant drainage into the stomach or intestine either by subsequent implantation of an external fistula or by primary anastomosis of such a wound to an opening in the alimentary tract. Wood in 1916 collected fifteen such cases of primary anastomosis with at least temporary improvement in some of the patients. Hemorrhage, peritonitis, and insufficient biliary drainage were the complications most frequently responsible for failure of these attempts. In recent years such methods have been generally abandoned in favor of more reliable techniques. The anastomosis of an external intrahepatic biliary fistula to the jejunum by Carter and Marradino<sup>2</sup> in 1944 is the only successful case of this kind found in the recent literature.

The procedure presented in this paper is designed to drain the intrahepatic biliary system directly into the intestinal tract either in the distal ileum or in common with these previously suggested in the jejunum.

#### DISCUSSION

A new method is presented of treating atresia and obstruction of the intrahepatic biliary system, the treatment of which has hitherto been unsatisfactory. In anastomosing one of the intrahepatic biliary ducts to the jejunum





Fig. 10.—Dog's liver and attached jejunum, the probe passing through intrahepatic cholangiojejunostomy. The common duct had been ligated and the gall bladder removed prior to the performance of this anastomosis. There is moderate dilatation of the extrahepatic biliary system.



Fig. 11.—Photomicrograph of intrahepatic cholangiojejunostomy, showing mucosa-to-mucosa healing.

an intrahepatic duct large enough so that a direct end-to-side anastomosis may be performed and the chances of maintaining the patency of such an anastomosis are much better than in the implantation procedures used in infant. The intrahepatic jejunal anastomosis will of course be subject to all of the complications, such as stenosis, ascending infection, and so forth, that occur in anastomoses between the extrahepatic biliary system and the alimentary tract. Certain features of the procedure have been mentioned which might lessen the incidence of such complication when an intrahepatic duct is used.

The procedure has been carried out in dogs to study the performance of the anastomosis and its effect on the liver and remaining duct system. In the animal from which specimens were obtained for Figs. 10 and 11 the common duct was doubly ligated and divided and the gall bladder removed. One week later the major portion of an anterior lobe of the liver was excised and the proximal end of the principal duct anastomosed to the side of a jejunal loop. An enterocentrostomy was performed between the two limbs of the jejunal loop. Two months later at the time the animal was killed, it was in good health, there was no jaundice and the stools were of normal color. The anastomosis between the bile duct and the jejunum was patent and well healed without evidence of stricture. There was moderate dilatation of the extrahepatic biliary system. The mucosa of the jejunal loop was covered with bile-colored fluid. The duct used in this experiment was considerably smaller than that found in the adult patient previously described. Such experimental results support our view that intrahepatic biliary duct may be used for biliary drainage. Further experimental studies are in progress.

Previously the only attempts have been made to divert the contents of the intrahepatic biliary system directly into the alimentary tract by resecting a small portion of the free jejunal edge and inserting a cannula or a probe into the liver substance and then directing the resultant drainage into the duodenum or intestine either by subsequent implantation of an external fistula or by primary anastomosis of such a wound to an opening in the alimentary tract. Thomas<sup>10</sup> in 1914 collected fifteen such cases of primary anastomosis with at least temporary improvement in six of the patients. Hemorrhage, peritonitis, and insufficient biliary drainage were the complications most frequently responsible for failure of these attempts. In recent years such method has been generally abandoned in favor of more reliable techniques. The anastomosis of an external intrahepatic biliary fistula to the jejunum (Carr and Marraschino<sup>11</sup> in 1944) is the only successful one of this kind found in the recent literature.

The procedure presented in this paper is designed to be in the intrahepatic biliary system directly into the intestinal tract and it is the only one that has in this regard in common with these previously suggested methods.

#### DISCUSSION

The method presented of treating extensive obstruction of the extrahepatic biliary system, the treatment of which has hitherto been unsatisfactory by anastomosing one of the intrahepatic biliary ducts to the jejunum

following a partial resection of the left lobe of the liver. It should be emphasized that although our experience with the procedure has been encouraging it has been limited both clinically and experimentally and the final evaluation must await further clinical observations.

## ADRESKRIJVEN

Since this paper submitted for publication the procedure has been carried out in the case of an additional adult patient. In both, complete biliary drainage has been obtained. A large intraperitoneal abscess, presumably resulting from previous exploration, was incidentally opened during the operation on one of these patients and her postoperative course has been difficult and prolonged. Drainage of numerous intraperitoneal abscesses has been reported. The ileo-falce at the intestinal tract, however, has been unmanipulated.

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## A NEW METHOD FOR SURGICAL TREATMENT OF LARGE OMPHALOCELES

ROBERT E. GROSS, M.D., BOSTON, MASS.

(From the Department of Surgery of the Children's Hospital and the Harvard Medical School)

**B**ECAUSE of differences in prognosis and surgical treatment, an omphalocele must be distinguished from the usual form of umbilical hernia. The latter condition is frequently encountered in childhood and is characterized by a defect of small or moderate size in the rectus fascia and muscles of the navel area, so that a peritoneal sac bulges forward and is covered only by skin. In contrast, an omphalocele is a congenital abnormality in which there is a wide separation of the fascia and muscles in the central part of the abdominal wall and the bulging peritoneum (amniotic membrane) has no cutaneous covering. Omphaloceles have such thin-walled sacs that they are likely to rupture in the first hours or days of life, abdominal perforation is a grave or fatal complication. To avoid such catastrophes, omphaloceles should be operated upon immediately after birth, and indeed it is preferable to repair them in the first hours, before the child has swallowed or drunk which distend the gastrointestinal tract and thereby increase the surgical difficulties at the operating table.

Omphaloceles vary greatly in size. The smaller ones are no more than a centimeter in radius in size. The largest ones are 1 to 1.5 cm. in diameter and we have a larger volume capacity than the child's main abdominal cavity. There is all ranges in size between these two extremes. Small or moderate sized omphaloceles usually enclose only a few loops of intestine but the larger ones contain more of the hollow viscera and in addition, a considerable part of the liver. Depending from the apex of the sac or from the inferior surface of the same, there arises the umbilical cord. From the cord the umbilical vein and the two umbilical arteries branch out over the surface of the omphalocele sac to reach the margin of the abdominal wall above and below.

Omphalocele represent an arrest in development of the abdominal cavity and wall during the third month of fetal life. During that early period the embryo in its normal position has a forward extension into the flared-out base of the amniotic sac, so that a large part of the intestinal tract is displaced anteriorly into this recess. At a later time the abdominal cavity grows at an accelerated rate and becomes large enough to receive all of the abdominal viscera which are withdrawn into it simultaneously the inferior abdominal wall becomes completely formed and the various fasciae and muscles meet and join in the midline. If this normal series of events and development go with the abdominal wall does not grow fast enough and some abdominal viscera will remain in the base of the umbilical cord—protruding through a large defect in the abdominal wall and encircled by a thin-walled sac.

If omphaloceles are small, there is no real surgical problem in repairing them; it is a simple matter to close the sac completely, replace loops of intestine within the abdominal wall and bring together the various layers of the abdominal wall.

following a partial resection of the left lobe of the liver. It should be emphasized that although our experience with the procedure has been encouraging it has been limited both clinically and experimentally and the final evaluation must await further clinical observations.

#### ADDENDUM

*Since this paper submitted for publication the procedure has been carried out in the case of two additional patients. In both, adequate biliary drainage has been obtained. A large intraperitoneal abscess, presumably resulting from previous exploration, was inadvertently opened during the operation on one of these patients, and her postoperative course has been difficult and prolonged. Drainage of numerous intraperitoneal abscesses has been required. The flow of bile into the intestinal tract, however, has been undisturbed.*

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## A NEW METHOD FOR SURGICAL TREATMENT OF LARGE OMPHALOCELES

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**B**ECAUSE of differences in prognosis and surgical treatment, an omphalocele must be differentiated from the usual form of umbilical hernia. The latter condition is frequently encountered in childhood and is characterized by a defect of small or moderate size in the rectus fascia and muscles of the navel area so that a peritoneal sac bulges forward and is covered only by skin. In contrast, an omphalocele is a congenital abnormality in which there is a wide separation of the fasciae and muscles in the central part of the abdominal wall and the bulging peritoneum (amniotic membrane) has no cutaneous covering. Omphaloceles have such thin walled sacs that they are likely to rupture in the first hours or days of life; abdominal excoriation is a grave or fatal complication. To avoid such catastrophes, omphaloceles should be operated upon immediately after birth, and indeed it is preferable to repair them in the first hours, before the child has swallowed air or milk which distend the gastrointestinal tract and thereby increase the surgical difficulties at the operating table.

Omphaloceles vary greatly in size. The smaller ones are no more than 3 cm. in cross diameter. The largest ones are 10 to 15 cm. in diameter and may have a large cubic capacity than the child's main abdominal cavity. There are all degrees in size between these two extremes. Small or moderate-sized omphaloceles usually enclose only a few loops of intestine, but the larger ones contain more of the hollow viscera and, in addition, a considerable part of the liver. Leading from the apex of the sac is a cord from the inferior surface of the same thence arises the umbilical cord. From the cord the umbilical vein and the two umbilical arteries branch out over the surface of the omphalocele sac to reach the margins of the abdominal wall above and below.

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If omphaloceles are small, there is no real surgical problem in repairing them; it is a simple matter to excise the sac completely, replace loops of intestine within the abdomen and bring together the various layers of the abdominal wall.



closure of the abdominal wall is a reasonably satisfactory attack on the problem because it avoids the production of high intra-abdominal pressure. The drawbacks of such an undertaking (with excision of the sac and covering the intestines with skin only) are obviously twofold. First the repair is extremely weak and gives rise to considerable anxiety during the first week or ten days following the initial operation because of fear that the cutaneous suture line will not heal. Second, the intestines are covered by a very broad surface which is raw and to which they may become densely adherent.

To obviate the two drawbacks indicated in the last paragraph, I would like to suggest herewith a two-stage operation which to my knowledge has not been performed before. The essential feature of this therapy is to leave intact the omphalocele membrane (dirty though it might seem to be) cut free and widely undermine the surrounding skin and then bring together these huge cutaneous flaps anteriorly to cover over the bulging omphalocele sac. By this maneuver the intestines are covered by a smooth membrane which resembles a normal peritoneum; the intestines have not been exposed to the air nor have they been touched by any instrument or gauze and the pressure within the abdominal cavity has not increased appreciably. Furthermore the combination of intact omphalocele membrane and superimposed skin forms a stronger wall than was provided by the old operation in which only skin was brought together over the intestines. While the child may be left with a huge bulging and weird-looking mass on the anterior abdominal wall, this is compatible with life and will permit a secondary repair some months later when the abdominal cavity has grown sufficient to receive easily the intestines and permit a closure of the muscular fasciae. The soundness of these principles is demonstrated by Cases 1 and 2 in which both stages have been completed, and also by Case 3 in which the primary stage has been done but the secondary repair has not yet been undertaken. I am reasonably sure that in all three of these infants a fatal outcome would have followed an attempt at a one-stage repair of the omphalocele in the newborn period.

The two-stage procedure herein proposed would appear to have certain hazards, none of which however materialized in our three patients. First, the omphalocele sac is obviously not sterile and to bury it (minus the stump of the cord) beneath the skin carries certain risks of infection. Yet a careful cleansing of the same followed by application of half strength tincture of iodine (tincture of iodine diluted with an equal volume of 70 per cent alcohol) was sufficient to sterilize it in our three patients. Second, it is possible that wind and raining and mobilization of skin might lead to sloughing particularly when the cutaneous flaps are applied to the underlying membrane which has no important vascularity. However this has not proved to be troublesome. Third there is some possibility that the amniotic mesoderm might not grow to the skin which is applied to it but instead that fluid might accumulate between these two layers and form cysts which would be difficult to treat. No cystic accumulations occurred in any of the three cases here reported. Possibly the tincture of iodine solution caused sufficient reaction to destroy the smooth external surface of the amniotic sac a process which might not have occurred if a mild type of anti-



to make a sturdy repair. In distinct contrast large omphaloceles present formidable surgical problem and is attended by high fatality rates. When herniation is great the surgeon will find that the abdominal cavity is relatively small and will not receive the various displaced viscera and simultaneously permit a satisfactory closure of the abdominal wall. In a series of sixty babies treated for omphalocele at the Boston Children's Hospital a review of the material shows that the size of the omphalocele sac has won prognostic value. In those patients with a sac less than 5 cm in diameter there was about a 75 per cent chance of survival following surgery. When the sac was 7 to 9 cm in diameter survivals were cut to about 30 per cent. When the sacs were larger than 9 cm the survivals were reduced to about 15 per cent. Whenever a large portion of liver was found in the omphalocele a grave outlook could be expected.

The generally accepted therapy for omphaloceles has consisted of eversion of the sac (with the attached stump of cord) replacement of intestines and other viscera into the abdominal cavity and attempt at some sort of repair of the abdominal wall. In cases with small or medium sized omphaloceles, the edges of the peritoneum, the rectus muscle and the rectus fasciae can be brought together in the midline for suitable closure. When omphaloceles are large it has been difficult to push the viscera back into the small abdominal cavity and then complete the abdominal wall repair. There is a continual battle, often somewhat brutal while trying to pack intestinal loops into a cavity which is too small to receive them. By continued effort the surgeon may be able to crowd intestines back into the abdomen, and repair the musculofascial layers, only to have a fatality within twenty-four or fifty-eight hours after operation. Severe crowding of viscera into the abdominal cavity is apt to give rise to three serious and fatal complications. First the diaphragm may be pushed upward so that untolerable respiratory distress and even cyanosis appear. Second, great pressure on the inferior vena cava can impede the return flow of blood from the lower abdomen and legs so that circulatory collapse and even death supervene. Third, compression of the stomach and intestines may give rise to temporary obstruction. In short the surgeon while having spared the baby from rupture of an omphalocele is faced with the dilemma of a baby in the postoperative period who cannot breathe satisfactorily, who has great obstruction of the venous circulation and whose gastrointestinal tract has an impaired function because of the high intra-abdominal tension.

If fatality rates in the treatment of large omphaloceles are to be reduced, it is essential to devise some method whereby the intra-abdominal crowding is avoided at the first operation. In previous communication mention is made of one case in which the omphalocele sac was excised and it appeared to be impossible to get the muscles and fasciae together without undue tension; therefore, only the skin and subcutaneous tissues were brought together over the intestines. Such a type of repair might seem inadequate but during the ensuing weeks the child's abdominal wall will become stretched and it is then possible to undertake a secondary repair for closure of the muscles and fasciae. This general principle of a two-stage repair of the abdominal wall has been previously set forth by Ladd and Gross. A limited experience has indicated that a two-stage

## CASE REPORTS

C 11-1 (1) A entered the hospital Jan. 1941 (10 hour) stage for treatment of large osteophorite. The b.b. weighed pounds 4 ounces. The enormous osteophorite, the general shape and size of which had been judged from the drawing in Fig. 1. The osteophorite was an intact transparent and quite thin. Through it could be seen numerous loops of intestines and large vessels. In the upper part of the tumor a large portion of the liver extended to be about 1/3 of the liver volume. The present size, extended somewhat larger or probably somewhat larger than the general lateral wall. No other malformations were noted.

[illegible]

For next four hours of operation the infant kept high concentration on vision and used a gesture which is employed after the time of water are given every few hours. It is assumed that the infant is able to do the work of a normal child one or two years of age in 13 months every 24 hours. On the third postnatal day infant with malnutrition as a result of the mother's diet is brought out through a hole in the wall of the full formula being less than 1 month old. The mother is now one month old on the eighth postnatal day. There was no further feeding. The central part of the head of the infant is marked with a permanent ink on the back of the head of the infant. A sterile dress is put on the infant. The infant is now in the hospital and is employed for a week.

For the 1st thing right away is I both was extremely frequent during it and the internal functions are quite satisfactory. The last fed all, and did not seem to me y distress (slept, he I also appeared to quite comfort him in spite of the fact that he presented nothing (physical) more. I b c all of us justify g t the parents.

septic had been employed. Fourth, it is possible at the first operation when the skin is cut away from the base of the sac for raising of the cutaneous flap, that small islands of epidermis may be left on the base of the sac and covered up—which theoretically could give rise to subsequent inclusion cysts. This objection has minimal importance since it is possible to remove such inclusion cysts during the secondary operation. Fifth, it is theoretically possible that a strong antiseptic might penetrate the thin amniotic membrane and set up adhesions between its inner surface and the adjacent intestines. However, in the first two cases, the secondary operation has now been done and no intra-abdominal adhesion has been found.

The experiences herein reported are limited, but they would seem to indicate that the largest omphaloceles can be successfully treated by this new technique. More cases will be necessary in order to give a better estimate of the duration of time which is necessary between the first and second operations. In the first case ten months elapsed between the two stages, and at the time of the second operation the abdominal cavity was large enough and the abdominal wall was lax enough to permit a very satisfactory repair. The second patient weighed but 3  $\frac{1}{2}$  pounds at birth, and certainly any other type of operation which would have greatly increased intra-abdominal tension would have been a fatal form of therapy. The secondary operation for this child was undertaken at the age of 6 months and although all the viscera were replaced into the abdominal cavity the abdominal wall repair was made under some tension. Therefore I had the distinct impression that a further delay of a few months would have made the repair much easier. In the third patient six months after the primary operation the secondary operation still being delayed because of tenderness of the protruding mass. In short the secondary repair can probably be done from six to twelve months after the initial operation and the time interval must be determined in any given case by the irritation caused by the infant's general abdominal activity. When manual pressure on the bulging mass shows that the viscera can easily be pushed back into the abdominal cavity and when the sac wall can be picked up readily between the examining fingers (Fig. 3 B) then the appropriate time has arrived for the secondary operation.

It is not necessary to hospitalize babies between the first and second operations. It has been possible in all three of these cases to discharge the children as soon as there is cutaneous healing after the first operation. Naturally the mother has been apprehensive at first about the appearance of the enormous, bulging mass on the abdomen but in each instance the parent is very well satisfied by a careful explanation of what was being attempted, backed up with the assurance that the mass would not rupture. Normal feeding and bathing regimes were permitted. Babies were allowed to be picked up at any time and were treated like normal youngsters. No attempt was made to prohibit them from straining or crying even though these activities momentarily increased the size of the abdominal mass. The bulging structure was given some slight support by wrapping the baby's torso with a elastic type of bandage for which a piece of 6 inch wide ace bandage served admirably.

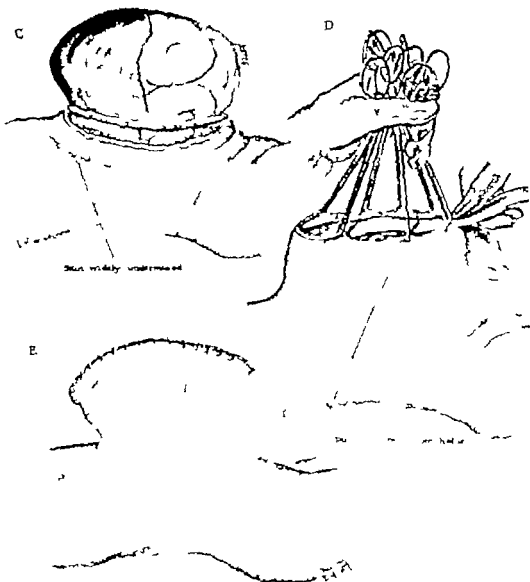


Fig. 1.—Fracture operation continued. C shows the wide, shallow incision made in the conjunctiva and sclera. D shows the removal of the tumor and the underlying tissue. E shows the large, curved incision made in the conjunctiva and sclera.

The skin of the rat used in good condition and seemed to have an adequate circulation. To be bathing permitted. After the sixth week dressings were discontinued, but slightly elastic bandage kept round the belly hole except for short periods when the rat being bathed. For the next 10 days the skin of the belly was wrapped several times around the body and seemed to be doing best. During the first six months of life the presenting mass was always quite easy manual pressure over it gave the impression that there

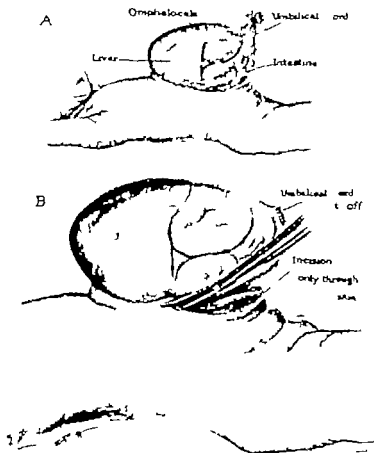


Figure 1. Operation. (Drawing of omphalocoele (from Case 1) shown but larger than as presented in the photograph of the omphalocoele)

could not yet be displaced back into the abdomen. During the seventh month it was noted for the first time that the presenting mass was beginning to get softer and less tense. By the eighth month there was considerable flaccidity of the abdominal wall and by manual compression the various organs could be pushed back and almost contained within the general abdominal cavity. By the tenth month there was great flaccidity of the skin and with very little effort the intestines and the liver could be displaced backward into the abdomen, and

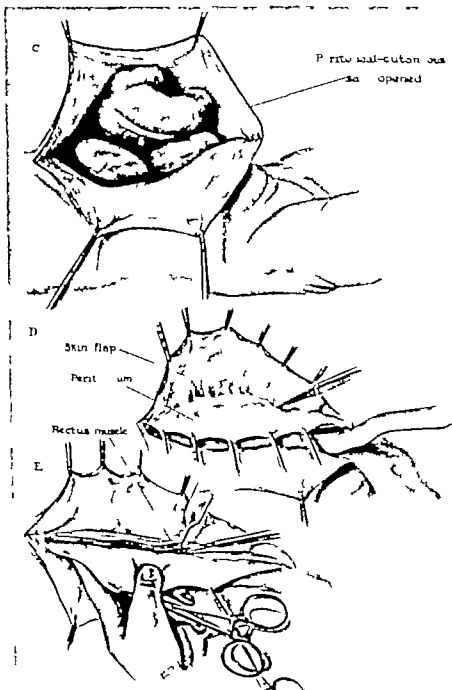


Fig. —Secondary operation continued. C This sec opens, showing lack of adhesion between ca. and inferior of he. D Left abd. of abdomen 1 all the held so that peritoneal muscle is to be added, not isolated.

they could be held down below the level where normal bladder wall should be. How-  
 ever, it was decided to perform the secondary repair at this time.

The baby reentered the hospital Oct. 20, 1941. The weight was 10 pounds, 10 ounces.  
 The appearance of the bladder is indicated by Fig. 3 C. The general condition of the child  
 was excellent. For thirty-six hours, preoperative preparation consisted of constant gastric  
 suction and the use of tent catheters, high concentration of oxygen, keeping by these two  
 steps to distend the intestines and to flatten the subsequent surgical procedure.

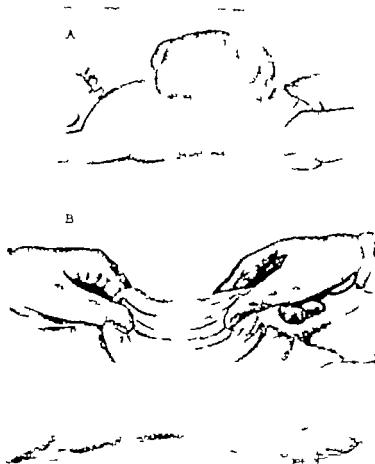


Fig. 3—Secondary operation. A: Preoperative view of the bladder-covered in vaginal hysterectomy of second operation (6 months of age). B: Intraoperative view of the bladder. The bladder is shown squeezed and held into the pelvic cavity, but the bladder is not yet attached and its position demonstrated.

Secondary operation was carried out October 22, under ether anesthesia. A median  
 incision was made over the pubis of the mother, entering the incision through the skin and the  
 underlying peritoneal membrane. Introducing fingers and the abdomen, this opening was  
 carried upward to the exposed and down to the pelvis. The incision was then  
 carried forward between the two surfaces of the bladder and the surrounding tissues. The subse-  
 quent steps in the repair are illustrated in Figs. 4, 5, and 6. The next steps in this re-

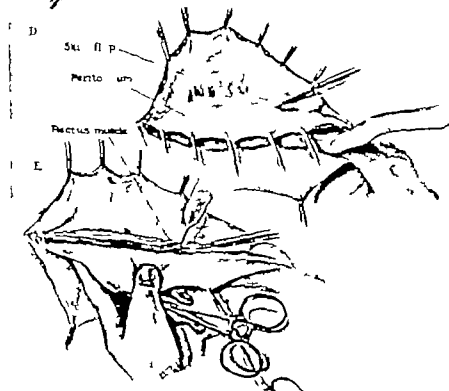
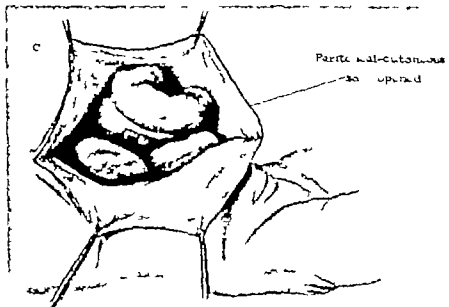


Fig. 1. Secondary operation method. C This incision is made above the left side of abdomen. The skin and lower part of the muscle can be separated from skin. D Separation of the connective tissue and left



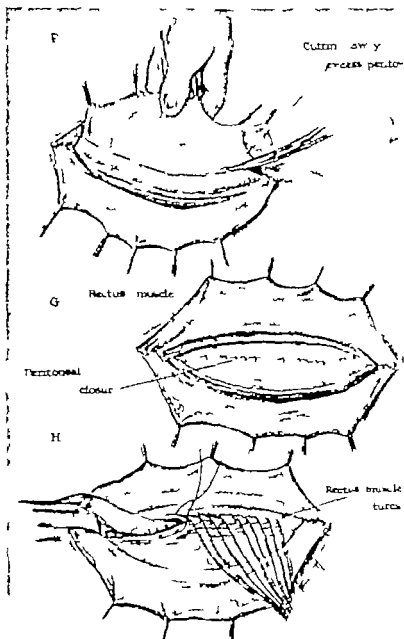


Fig. 1.—Secondary operation technique. F. Right side of the abdomen, not yet closed. G. Peritoneum easily closed. H. Rectus muscle turned and sutured. The interrupted silk suture.



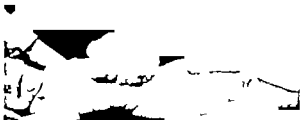
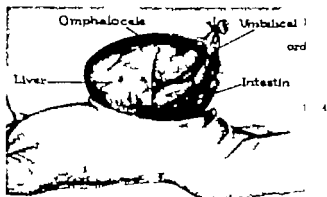


FIG 1.—Stages in the omphalocele repair (Case 1). *A* Drawing of original lesion before operation. The protruding mass is about the size of an, or possibly little larger than, the general abdominal cavity. *B* Photograph two weeks after first stage operation. *C* Photograph nine months after first operation, and immediately before second stage operation. *D* Photograph two months after completion of the second stage operation.

lyer and that there had been no formation of cyst or accumulation of fluid between them.  
 1. Liver. Second, no intra abdominal adhesions are present. Third, few small cutaneous tags which had been buried (at the first operation) could now be trimmed away and discarded.

The infant was kept in oxygen tent for three days following the operation and gastric suction as employed for thirty six hours. At no time was there any evidence of respiratory distress, or was there any evidence of venous congestion in the legs which would suggest excessive pressure on the inferior vena cava. On the third day small feedings were started and were taken well. These were increased in volume and caloric value gradually so that by the end of the fifth day full formula was being fed and being taken well. The cutaneous surfaces are removed on the seventh postoperative day and there was excellent healing of the wound. The patient was discharged from the hospital on the tenth day examination at that time showing well healed abdominal wall, without any evidence of muscular or fascial defect. Follow up carried out for three months after operation showed the infant to be in excellent condition. A photograph taken six months after operation is shown in Fig. 7 D.

Fig. 7 D

CASE 2.—Baby girl N being one of twins, entered the hospital May 26, 1947 at the age of 1½ hours. The baby weighed 3 pounds, 3 ounces. The general size and shape of the omphalocele is best appreciated by glance at Fig. 8 A. A long segment of umbilical cord was attached to the mass. The omphalocele was roughly 8 cm. in diameter and was covered by thin, translucent moist membrane. It contained numerous loops of intestines and small segment of liver in its upper border. Except for the omphalocele and the tiny area of the umbilicus, the remainder of the examination showed no abnormality.

Operation.—undertaken by the resident surgeon, under cyclopropane anesthesia. The umbilical sac carefully incised with either and then painted with half strength tincture of iodine. While it might have been theoretically possible to reduce the omphalocele outside the sac and then repair the abdominal wall, it was felt that in such small baby any increase of intra abdominal pressure could probably be followed by fatal result. Therefore the same type of procedure as has been outlined for Case 1 was decided upon. The long segment of umbilical cord was removed and the stump suitably ligated with silk sutures. Extensive skin flaps are then prepared as described in Case 1 and illustrated in Figs. 1 and 2. These generous flaps are brought up over the omphalocele and the opposing margins are united with layer of substantial silk sutures followed by layer of interrupted cutaneous silk stitches. The infant tolerated this operation rather poorly and the temperature fell to 97 F but with prompt measures the circulation was improved and the temperature was restored to normal. Following operation, the patient was kept in Chappell bed where the abdominal wall and organs are held in optimum position. Constant gastric suction was used for thirty six hours. Oral feedings were started cautiously and were raised to full caloric and volume requirement by the sixth day. In perinatal records, the infant was given penicillin and sulfadiazine for ten days. The cutaneous sutures were removed on the eighth day. There was no sloughing of the cutaneous flaps. For use of penicillin the infant was kept in the hospital for an extended period of time and was finally discharged on the twenty sixth day weighing 4 pounds, 6 ounces.

The baby followed from time to time in the outpatient department. Her progress satisfactory. At no time was there any evidence of respiratory embarrassment or of venous congestion in the legs. There was gradual gain in weight. The infant seemed to be quite comfortable. For the first four months the protruding abdominal mass remained rather small. An elastic abdominal binder was constantly used except for periods when the infant was being bathed. During the fifth month the skin of the sac appeared to be getting more lax and by the end of six months it was possible to exert compression, to displace all of the abdominal organs back into the abdominal cavity with only a slight pressure. It was therefore decided to undertake the second operation at this time.

The baby entered the hospital Nov. 16, 1947. She was in an excellent general condition. The weight was 11 pounds, 15 ounces. The general appearance of the abdomen and

cephalorule are shown in Fig. A, B. A thirty-six hour period of preparation was employed, during which constant gastric suction was used and the baby was placed in an oxygen tent carrying high concentrations of oxygen, utilizing these two steps as measures to deflate the intestines. On November 19, secondary operation was undertaken under ether anesthesia. The same steps were employed as was used in Case 1, and as illustrated in Figs. 2, 4, 5, and 6. The repair entirely satisfactory and it was possible to get accurate closure of the per-



Fig. 2.—Figures in the cephalorule repair (Case 2). A. Preoperative photograph of cephalorule in preparation for and during 3 hours of oxygen. B. Photograph six months after primary operation, and immediately before the secondary repair. C. Photograph for the secondary repair of the bilateral wa.

to remain, and the layer anterior rectus of muscle and the skin. However, the area of the and the skin were under considerable tension and were not completed in the same way as that of the other side. (The area of the skin had been left open.)

At the time of the operation, the infant was under ether anesthesia, and the respiration was maintained by the use of a respirator. A roentgenogram of the chest showed the diaphragm to be



13 pounds, the general abdominal cavity is still believed to be too small to receive all of the intestines—a point which further convinces us that any hasty attempts in the neonatal period to crowd viscera back into the abdomen could certainly have been followed by fatality. There seems to be little doubt, however, that if the infant is allowed to grow for a few months more the abdominal cavity will eventually become large enough to receive these viscera and permit satisfactory repair of the muscles and fasciae of the abdominal wall.

#### SUMMARY AND CONCLUSIONS

A surgical method is described for the treatment of large omphaloceles. Experiences with the method are summarized by the notes from three cases in which it has been employed. The abdominal wall is repaired by a two-stage technique, the essential feature of the first stage being the preservation of the amniotic membrane and covering this with wide skin flaps, making no attempt to crowd the viscera back into the small abdominal cavity. In this way it is possible to avoid the devastating effects of a high intra-abdominal pressure which resulted from most of the types of surgical repair which have been previously employed and described in the literature. By the present technique the abdominal cavity is allowed to increase in size during the ensuing six to twelve months, at the end of which time the various viscera can be replaced easily into the abdomen and the anterior abdominal wall can be completely repaired by bringing together the various fascia and muscle layers. By this newer two-stage technique it should be possible to repair the largest of omphaloceles and to reduce greatly the mortality rates which have previously accompanied the treatment of these malformations.

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# THE HERNIA PROBLEM WITH REFERENCE TO A MODIFICATION OF THE McVAY TECHNIQUE

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A PRUSAL of current literature<sup>1-12, 14, 15</sup> indicates an increasing dissatisfaction on the part of many surgeons with standard methods of inguinal hernia repair. The classical operations of Halsted<sup>3</sup> and Bassini<sup>4</sup> are probably still the more frequently employed methods today although critical anatomic studies<sup>10, 11</sup> emphasize that they are incompatible in concept with modern description of fascial and aponeurotic continuities of the inguinal strata. It is the purpose of this communication to outline the policies upon hernia as employed in the teaching program for residents at the Birmingham Veterans Administration Hospital, and to describe a minor modification of the Cooper's ligament technique as described by McVay and Anson<sup>12, 13</sup> and Harkins.<sup>6</sup>

## INDIRECT INGUINAL HERNIA

In direct hernias, particularly in young people are best dealt with by simple excision and transfixion of the hernial sac with minimal disturbance to either the cord or the floor of the inguinal canal. Operations designed to suture the various inguinal layers to the inguinal ligament detract from the end results inasmuch as they weaken the defenses against recurrence (particularly in the form of direct and femoral hernia). Recurrences in uncomplicated indirect hernia are rare. This has been emphasized by Hognet<sup>14</sup> in his statement that in "consecutive operations of indirect hernias in children, not a single recurrence had developed. Recurrences in indirect hernia, when they occur are frequently the result of technical errors in dealing with the sac or in failing to provide for reinforcement of the dilated internal ring. As will be discussed later the complicated indirect hernia with attenuation of the floor of the inguinal canal provides a surgical problem which is analogous to direct hernia. The most significant evidence against Bassini method is the vast number of modifications that surgeons have thought it necessary to adopt in order to improve results. There is little evidence to support the view that any of the modifications give better results than the original.

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History of the  
it will be an



15 pounds, the general abdominal cavity is still believed to be too small to receive all of the intestines—a point which further convinces us that any heroic attempts in the neonatal period to crowd viscera back into the abdomen would certainly have been followed by fatality. There seems to be little doubt, however, that if the infant is allowed to grow for a few months more the abdominal cavity will eventually become large enough to receive these viscera and permit satisfactory repair of the muscles and fascia of the abdominal wall.

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A surgical method is described for the treatment of large omphaloceles. Experiences with the method are summarized by the notes from three cases in which it has been employed. The abdominal wall is repaired by a two-stage technique, the essential feature of the first stage being the preservation of the amniotic membrane and covering this with wide skin flaps, making no attempt to crowd the viscera back into the small abdominal cavity. In this way it is possible to avoid the deleterious effects of a high intra-abdominal pressure which resulted from most of the types of surgical repair which have been previously employed and described in the literature. By the present technique the abdominal cavity is allowed to increase in size during the ensuing six to twelve months, at the end of which time the various viscera can be replaced easily into the abdomen and the anterior abdominal wall can be completely repaired by bringing together the various fasciae and muscle layers. By this newer two-stage technique it should be possible to repair the largest of omphaloceles and to reduce greatly the mortality rates which have previously accompanied the treatment of these malformations.

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recurrence incidence of 23 per cent 27 per cent and 28 per cent for direct hernia

When operating for recurrences (after a Bassini procedure) it is frequently apparent that there is no evidence of union between the muscle mass (conjoined tendon) and Poupart's ligament. Stein<sup>22</sup> has very ably stated that suture of the conjoined tendon to Poupart's ligament is fallacious because (1) there is no weakness in the floor of the canal; (2) nowhere in human economy is muscle used as a buffer state—it has four functions, namely motion locomotion control and stabilization (3) muscle fixation is bound to result in atrophy from inactivity and if separation eventually occurs, the muscle layer is weaker than before. About 77 per cent of the recurrences noted in British military hospital did not come through the posterior wall of the canal but through the internal ring.

The critical point in uncomplicated indirect hernia is not in the floor of the canal. Therefore operations designed to re-enforce the floor of the canal are ill considered. While serving with the British Army we were reluctantly employed the Bassini repair because in their opinion it gave unsatisfactory results, was inconsistent with physiologic and anatomic principles, and did not safeguard against the critical point of recurrence. To follow several hundred of these patients through a complete convalescence from the operating table to a time (six weeks later) when they were negotiating a most strenuous obstacle course was convincing enough to convert a skeptic. As soon as this principle was followed the incidence of recurrence was significantly reduced in British military surgery.

The technical aspect of simple ligation need little comment. It is not necessary to open the external oblique through the external ring but rather to employ a shorter incision carried well up over the internal ring. The cremaster is opened as a separate layer and the sac is identified at its medial and anterior position. The sac and all fat attachment should then be completely exposed and transfixed. The practice of opening the sac in order to insert a finger for purposes of definition and then stripping the cord structures with gauze is unnecessary and traumatic. It usually shreds the cord and makes hemostasis difficult.

Straight line

Incised line  
The sac is just a with a living riculum of the lumen.  
But beneath the roof of the inguinal canal is potential. It is important how we repair the rent in the transverse fascia to preserve normal function and liberate the internal ring. The role of the internal ring in the defense against recurrence is well known. If there is an attenuation of the floor of the canal, nothing further is done. Nonabsorbable sutures (silk or cotton) are preferable to catgut. Patients may be ambulatory from the beginning.

This procedure has been employed by one of us (J. M. F.) for the past five years in the military service as well as in civilian hospitals, with a great deal of satisfaction.

Simple ligation of the sac is inadequate if the internal ring is dilated or if there is weakness of the posterior wall of the inguinal canal. A long-standing

While attached to the British Army (1943) in one of their large military hospitals, one of us (J. M. F.) was emancipated from the Bassini method and its modifications under the tutelage of Brigadier Harold Edwards, the Consultant Surgeon for the Southern Command. Edwards, with a keen interest in the problem of hernia, made some interesting observations upon the vast material available in the United Kingdom at that time. In one 600-bed military hospital alone there were 634 operations for hernia in a nineteen-month period. Of 1,300 recruits entering a recruiting center in July 1941, 143 had hernias. It was estimated that there were 2,000,000 hernias in the United Kingdom and the shortage of man power made it necessary to salvage all available individuals. In the British hospital previously mentioned (where one of us was attached) there were several wards exclusively devoted to hernia, and a surgeon's operating schedule frequently included eight hernia operations a day.

Before the war there were available figures (Table I) to illustrate the results of surgery in one of the large London hospitals (St Thomas). They appeared in two series and are based on operations upon London policemen.<sup>10</sup>

TABLE I

OPERATION	NUMBER	RECURRENTS	PERCENTAGE RATE (%)
1931			
V. repair	29	4	13.8
Fowler	141	31	21.8
Bassini	36	8	22.5
Other methods	4	—	—
Total recurrence			20.8
1942			
Simple excision	96	8	9.3
Pastore-Lefa repair	39	6	15.4
Other methods	17	3	17.6
Total recurrence			12.0

from original  
operation  
alone  
series

It is apparent from these figures that the results of simple ligation and excision of the sac were superior to other methods. While only 29 of 213 hernias were treated by simple ligation in the first series, 86 of 141 in the second series were treated by this method with an over-all reduction in recurrence rate of 8 per cent.

During a six-month period in 1942, there were 806 recurrent inguinal hernias repaired (in British military hospital alone) and it was estimated that this group represented only about 60 per cent of all recurrent hernias examined. At one hospital 10 per cent of 323 hernias were recurrent and at another 16.6 per cent of 79 cases.

In the United States, the most analyses of a large series of cases which had a follow-up test of time reveal recurrence in excess of 10 per cent in direct hernias, and 7 per cent in indirect hernias. Anliker and Bissel recorded an incidence of recurrence in direct hernia of 9 per cent. Others have recorded a



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TABLE I

OPERATION	NUMBER	RECURRENTS	PERCENTAGE RATE (%)
1831			
K repair	29	4	13.8
Fowler <sup>11</sup>	144	31	21.5
Flap	26	8	30.8
Other methods	4		
Total recurrence			50.8
1912			
Simple excision	86	8	9.3
Fascia lata repair	39	4	10.3
Other methods	17	3	17.6
Total recurrence			37.2

It is apparent from these figures that the results of simple ligation and excision of the sac were superior to other methods. While only 29 of 213 hernias were treated by simple ligation in the first series, 86 of 143 in the second series were treated by this method with an overall reduction in recurrence incidence of 5 per cent.

During a six-month period in 1841, there were 605 recurrent inguinal hernias repaired (in British military hospitals alone) and it was estimated that this group represented only about 60 per cent of all recurrent hernias examined. At one hospital 10 per cent of 126 hernias were recurrent, and at another 16.6 per cent of 78 cases.

In the United States most analyses of a large series of cases which had had adequate test of time reveal recurrence in excess of 10 per cent in direct hernias, and 25 per cent in indirect hernias. Andrews and Brack recorded an incidence of recurrence in direct hernia of 27 per cent. Others have recorded a

The McArthur operation (1904) differs from the original Bassini in that a pedicled strip of external oblique fascia is utilized to suture the conjoined structures to the inguinal ligament. Biward (1939) proposed the routine use of this operation in a child, and called special attention to incorporating the *ligamentum inguinale reflexum* to obliterate the defect between the pubic spine and the lowermost approximating stitch in the laval operations. In 1921 Gallie and LeMessurier<sup>1</sup> introduced repair of the posterior wall with interlacing strands of fascia lata.

A most significant contribution came in 1941 from the fundamental anatomic studies of McVay and Anson.<sup>2,3,4</sup> They emphasized the general misconceptions concerning the points of attachment of the inguinal layers. Briefly their studies may be summarized as follows:

1 The inguinal ligament at its inferior and lateral aspect is a marginal structure. It is entirely separate from the fascia of the thigh and is not attached to the internal oblique. It is held loosely in position by the surrounding fascia and may be shelled out of its fascial bed by a blunt instrument to become the free margin of an aponeurosis which extends between the anterior iliac spine and the pubic tubercle.

2 The internal oblique arises not from the inguinal ligament as commonly stated, but rather from the iliopectineal fascia.

3 The inguinal portion of the transversus abdominis arises from the iliopectineal, and inserts not into the inguinal ligament but to Cooper's ligament on the superior pubic ramus.

4 Suture of the transversalis fascia, transversus abdominis, and internal iliac to the inguinal ligament violates the surgical principle of restoring muscular fascial anal to normal. The inguinal ligament is not the inversion of any of these structures, and its relationship is simply one of contiguity.

#### TECHNIQUE OF COOPER'S LIGAMENT HERNIOGRAPHY

The principle of Cooper's ligament herniography for hernial repair has been employed by one of us (J. M. F.) since its original description. It has been employed on a surgical service of the University of Michigan, in both American and British military hospitals, and more recently it has been adopted on the surgical service of the Birmingham Veteran Administration Hospital. Suffice it to say that the operation is considered to be the best method to deal with large indirect hernias (with associated defect of the inguinal floor), direct hernias of an old description, recurrent hernias, and femoral hernias. It is considered to be superior to fascial transplants in recurrent hernia. During the past twelve months this operation has been carried out in six to two patients, the great majority by the resident of the Birmingham staff. Certain technical features

<sup>1</sup> When the rectus abdominis is cut and separated from the transverse iliac muscle, the inguinal ligament is pulled out of the sheath of the internal oblique muscle. It is then found to be a free margin of the fascia lata, and may be sutured to the inguinal ligament. The inguinal ligament is not the inversion of any of these structures, and its relationship is simply one of contiguity.

<sup>2</sup> It is composed of the internal iliac artery, the internal iliac vein, the internal iliac nerve, the internal iliac lymphatics, and the internal iliac vessels.

<sup>3</sup> The inguinal ligament is not the inversion of any of these structures, and its relationship is simply one of contiguity.

<sup>4</sup> The inguinal ligament is not the inversion of any of these structures, and its relationship is simply one of contiguity.

indirect hernia may so dilate the internal ring as to extend medially to the rectus sheath or inferiorly to the pulse tubercle, and thereby destroy the obliquity of the inguinal canal. When this occurs, the problem is the same as in direct hernia. There is then need for re-enforcement of the posterior wall. The most enthusiastic advocate of the simple ligation technique must, therefore, have an alternative procedure to deal effectively with an attenuated inguinal floor.

The standard criteria for differentiating direct from indirect hernia by physical signs are frequently unreliable. This is of utmost importance because the problems of direct and indirect hernia are just as unrelated as those of cholelithiasis and appendicitis. The best results in operations for hernia are achieved by the experienced surgeon because of his ability to recognize the variations in pathologic anatomy at the operating table. A small indirect sac with the patient recumbent and under general anesthesia may escape detection in the hands of the inexperienced, and in such instances it is easy to be guilty of self-deception in evaluating the tension and strength in the area of Hesselbach's triangle, so that an erroneous diagnosis of direct hernia is made. Recurrence will follow in the form of an indirect hernia. Femoral hernias are easily overlooked unless the transversalis fascia is incised so that the femoral canal can be exposed directly. So-called recurrent femoral hernias in some instances are overlooked femoral hernias.

These views are supported by the fact that most recurrences appear early after operation. Judd found 70 per cent of the recurrences in the first six months and 90 per cent in the first twelve months. Erdman found 73.9 per cent in the first twelve months and 98.6 per cent in the first twenty-four months. On several occasions we have seen recurrences (direct, indirect and femoral) as soon as the patient was allowed out of bed. In each instance the true nature of the inguinal defect had been overlooked at the primary operation, as demonstrated at a second operation. There perhaps is no other operation where a sound knowledge of the anatomic features involved is so important. Trainees in surgery are done a great injustice when allowed to begin upon this operation without experienced supervision. It is not uncommon to witness an experienced resident surgeon execute a skillful and carefully planned gastrectomy only to falter with indecision and apparent carelessness when dealing with an inguinal hernia. You can judge the worth of a surgeon by the way he does a hernia, and other similar quotations are legion.

#### INDIRECT HERNIA ASSOCIATED WITH DIRECT OR A LARGE INDIRECT HERNIA WITH LARGE DILATED INTERNAL RING DIRECT HERNIA

Where there is a need for more than simple ligation of the sac, what procedure are we to recommend? Since Baylis's original description in 1890<sup>1</sup> there have followed modifications too numerous to mention. Most of the modifications enjoying any degree of sustained popularity have embodied some type of fascial repair to supply bulk to the inguinal floor. Bloodgood in 1898 turned down a portion of the anterior rectus sheath and muscle and sutured them with the conjoined tendon and internal oblique to the shelving edge of Poupart's ligament.

many instances this incision will be actually through the attenuated fascia which makes up the direct defect. In smaller direct hernias it will be considerably lateral, and in this instance no effort is made to excise or ligate the direct sac. If it is unusually developed or protuberant a few inverting sutures may be used for inversion.

There is now access to the inside of the pelvis, and a rather large amount of preperitoneal fat will further preclude adequate exposure of the ligament. A narrow malleable retractor or a small Deaver retractor over an appropriate wood pad which is then be introduced through the defect in the transversalis fascia and deep into the pelvis. The preperitoneal fat can then be retracted superiorly in the direction of the femoral vein. At this point Cooper's ligament can be accurately visualized as well as the pectineus muscle and fascia. More often than not a small vein will traverse the ligament. An incision is then made in Cooper's ligament beginning at the pubic tubercle medially and carried out laterally to the substance of the pectineus muscle just short of the femoral vein. This layer of dense fascia can then be rotated upward and medially in the form of a flap, and will provide a freshly cut edge to accept sutures (Fig. 2). Thus

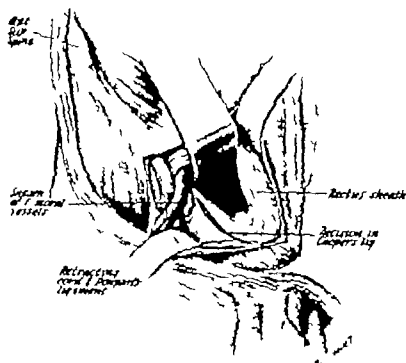


Fig. 2.—Incision has been made in Cooper's ligament. The exposed rectus sheath is then rolled up over the cord.



with comment only inasmuch as they incorporate one or two details which we believe may contribute to descriptions by McVay and later by Harkins. The follow up studies in this series have not been completed.

Exposure is obtained by a transverse incision made along the suprapubic fold. The external oblique cremasteric fascia and hernial sac if present are dealt with in the usual manner. The cord structures are then detached from the inguinal floor and retracted inferiorly together with the inguinal ligament. An incision is then made in the transversalis fascia about 1 cm from and parallel to the inguinal ligament. This incision is begun at the pubic tubercle and carried upward and laterally to a point just short of the epigastric vessels (Fig. 1). This step is essential to gain access to Cooper's ligament.

Many who have attempted this operation have had difficulty in utilizing Cooper's ligament for accurate suturing because of omission of this step. I

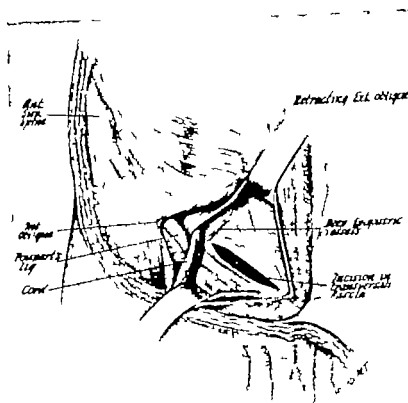


Fig. 1. The clear-cut incision on the floor of the inguinal canal. The internal ligament are retracted the incision opens out. Without the incision the incision is imperceptible. The incision is the incision in the transversalis fascia.

many instances this incision will be actually through the attenuated fascia which makes up the direct defect. In smaller direct hernias it will be considerably lateral and in this instance no effort is made to excise or ligate the direct sac. If it is unusually developed or protuberant a few imbricating sutures may be used for inversion.

There is now access to the inside of the pelvis, and a rather large amount of peritoneal fat will further preclude adequate exposure of the ligament. A narrow malleable retractor or a small Deaver retractor over an appropriate mesh pad should then be introduced through the defect in the transversalis fascia and deep into the pelvis. The peritoneal fat can then be retracted superiorly in the direction of the femoral vein. At this point Cooper's ligament can be accurately visualized as well as the pectineus muscle and fascia. More often than not a small vein will traverse the ligament. An incision is then made in Cooper's ligament beginning at the pubic tubercle medially and carried out laterally to the substance of the pectineus muscle just short of the femoral vein. This layer of loose fascia can then be rotated upward and medially in the form of a flap, and will provide a freshly cut edge to accept sutures (Fig. 2). This

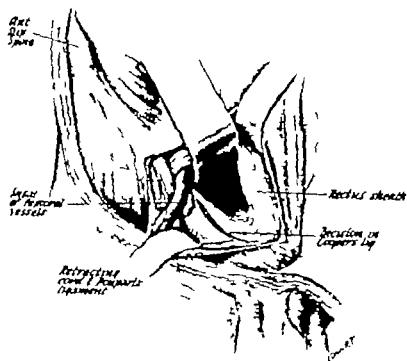


Fig. 2. An incision has been made in the Cooper's ligament extending up over the pectineus muscle to the level of the femoral vein.

modification of the original technique in our opinion offers certain advantages to suturing into the smooth surface of the ligament.

Several anatomic entities present themselves for suture to Cooper's ligament, depending upon their intrinsic state: the transversus abdominis aponeurosis and attached transversalis fascia, the internal oblique muscle and conjoint tendon, when present, the lateral border of the rectus sheath. In our opinion the transversalis layer is rarely satisfactory because it has been attenuated by the

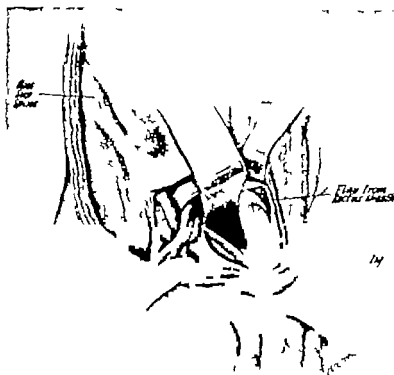


FIG. 2.—Illustration of the anterior abdominal wall. The external oblique muscle has been reflected and preserved to cover suboperatively the denuded rectus muscle. The margin of the thickened Cooper's ligament has been stirred up to accept suture.

presence of a direct hernia. The conjoint tendon is rarely tenacious, and the muscular portion of the internal oblique should not be used. We have frequently observed that residents have been forced to employ the lateral border of the rectus sheath, sometimes under the misconception that they were utilizing the conjoint structures. We have noted two recurrences following operation for direct repair and in each instance it was felt that the structures which had been utilized for suture to Cooper's ligament had failed to provide proper re-enforcement of the triangular direct defect.

Increasing experience indicates that in many instances the most satisfactory structure which is readily available is a triangular-shaped flap of the internal oblique and transversus component of the anterior rectus sheath. Contrary to anatomic descriptions the external oblique component may be separated almost to the linea alba. Elevation and preservation of the external oblique component of the rectus sheath afford adequate fascial covering for the denuded portion of the rectus nerve. The flap in the internal portion of the rectus sheath is

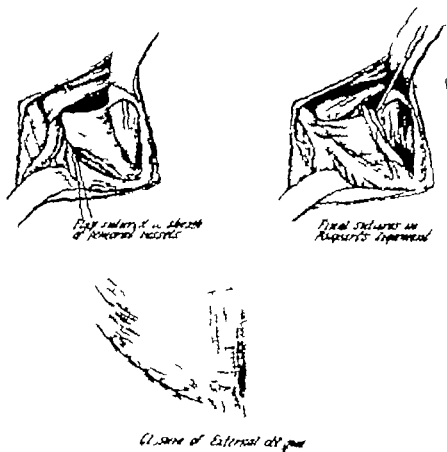


FIG. 1.—The rectus flap is turned down and sutured to the fixed Cooper's ligament. The line of suture extends up on the femoral sheath to the femoral ligament and interposes an extra layer of fascia into the pyramidal defect constituting the direct hernia. This may be accomplished without the aid of traction.

fashioned by inserting the insertion of the rectus tendon and carrying this line down upward to about the level of the internal ring and then outward to the lateral edge of the rectus sheath. The free edge of this flap is then rotated downward just as one would turn down the corner of a page in a book. This provides another fresh cut edge for accurate suture to the component previously fashioned

from Cooper's ligament (Fig 3). The freshly cut edges are then united by interrupted sutures. This line of suture will extend from the pubic tubercle below and medially to the femoral sheath above and laterally. The femoral ring is thereby obliterated. The transverse aponeurotic layer when available should also be included in this line of suture. The lateral angle of the base of the rotated triangular flap is then carried up and anchored to the inner border of the inguinal ligament so as to obliterate the defect at the internal ring. Occasionally a V-shaped incision at the base of the triangle is employed to allow the fascial flap to encircle completely the cord at the region of the internal ring. In this manner an extrafascial layer is interposed over the floor of the canal.

The external oblique is closed over the cord. In rare instances the medial edge of the external oblique has also been sutured to Cooper's ligament with anterior transposition of the cord. The fascial layers are sutured together with interrupted fine cotton or silk. (The relaxation afforded by the incision into the rectus sheath allows reconstruction without the slightest tension.) Continuous sutures of No. 30 stainless steel wire are employed for the subcutaneous layer and the skin. The latter is placed subcuticularly and both of them are removed on the seventh day.

This operation has proved satisfactory in all types of recurrent hernia. It has not been felt necessary to utilize autoplasmic fascial graft. In the present series there have been no wound infections, and two known recurrences (although follow up studies are incomplete). These recurrences are thought to be due to error in technique; in these two cases the standard McVay operation was used. To our knowledge no recurrences have occurred where the rotation flap of the internal component of the rectus sheath has been utilized.

This operation can be employed in bilateral hernias at a single sitting without fear of compromising the opposite side through undue tension.

#### SUMMARY AND CONCLUSION

1. Simple ligation of the sac is a satisfactory method for dealing with the uncommonly limited indirect hernia.

2. Complicated indirect hernias, direct hernias, recurrent hernias, and femoral hernias are best repaired with the Cooper's ligament technique.

3. A modification of the McVay technique is presented. Its advantages are discussed.

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from Cooper's Ligament (Fig. 3). The freshly cut edges are then united by interrupted sutures. This line of suture will extend from the pubic tubercle below and medially to the femoral sheath above and laterally. The femoral ring is thereby obliterated. The transversus aponeurotic layer when a suitable should also be included in this line of suture. The lateral angle of the base of the rotated triangular flap is then carried up and anchored to the inner border of the inguinal ligament so as to obturate the defect at the internal ring. Occasionally a V-shaped incision at the base of the triangle is employed to allow the fascial flap to encircle completely the cord at the region of the internal ring. In this manner an extrafascial layer is interposed over the floor of the canal.

The external oblique is closed over the cord. In rare instances the medial edge of the external oblique has also been sutured to Cooper's ligament with anterior transposition of the cord. The fascial layers are sutured together with interrupted fine cotton or silk. (The relaxation afforded by the incision into the rectus sheath allows reconstruction without the slightest tension.) Continuous sutures of No. 30 stainless steel wire are employed for the subcutaneous layers and the skin. The latter is placed subcuticularly and both of them are removed on the seventh day.

This operation has proved satisfactory in all types of recurrent hernia. It has not been felt necessary to utilize autoplasmic or vascular graft. In the present series there have been no wound infections, and two known recurrences (although follow up studies are incomplete). These recurrences are thought to be due to errors in technique; in these two cases the standard McVay operation was used. To our knowledge no recurrences have occurred where the rotation flap of the internal component of the rectus sheath has been utilized.

This operation can be employed in bilateral hernias at a single sitting without fear of complicating the opposite side through undue tension.

#### MEMORANDUM AND CONCLUSIONS

1. Simplification of the case is a satisfactory method of dealing with the uncomplicated indirect hernia.

Complicated and rect. hernias, direct hernia, recurrent hernia, and femoral hernias are best repaired with the Cooper's ligament technique.

3. A modification of the McVay technique is presented. Its advantages are discussed.

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cases of posttraumatic and other edematous states, and certain cases of hereditary paralysis. In such instances sympathectomy may yield results far better than one might reasonably have anticipated from the preoperative studies, but sometimes the results are equally disappointing. If the procedure is ever to be used, then more or less as a therapeutic trial, it is obviously important to know what hazards are associated with it.

This report is based upon a fairly extensive personal experience and upon careful analysis of the complications which followed operative sympathetic denervation of 813 extremities in 677 patients. The operative technique will be described in some detail. Only those data concerning the patient which have possible value next to the pericardial risk and to postoperative complications will be cited. The efficacy of sympathectomy in relieving the conditions for which it was performed will not be considered here. The results of sympathectomy in certain of these disorders have been reported elsewhere.

#### OPERATIVE TECHNIQUE

The operative techniques which Dr. associates and I have utilized represent in no sense an original contribution but are based upon the fundamental principles which have been previously described by others. It is hoped, however, that certain observations and minor modifications which I have found helpful in performing these procedures and in training my assistants to do them may prove of some usefulness to others.

*Lumbar Sympathetic Gangliectomy*—Lumbar sympathetic gangliectomy (omy) was performed at first through a rather cumbersome posterior incision. The transabdominal approach was utilized for a while, however it not only subjected the patient unnecessarily to an intraperitoneal operation but also proved unsatisfactory for proper exposure of the upper ganglia of the lumbar chain. Excellent descriptions of the anterior peritoneal exposure of the sympathetic chain through a muscle-splitting incision were reported by Flotho in 1893 and by Pearl in 1937. Subsequently more extensive anterior or flank incisions involving a partial transection of muscle layers have been advocated primarily on the basis of more adequate exposure of the upper portion of the sympathetic chain. From the beginning I have used an anterior muscle-splitting incision carried out essentially according to the suggestion of Elliott and Pearl.

Good muscular relaxation is essential and spinal anesthesia is employed unless there is some definite contraindication to its use. Since the operation is performed in a short period, premedication is sufficient and no longer-lasting anesthetic agent is required. Formerly those cases in which a general anesthesia was used frequently proved far from ideal. Lack of good relaxation of the muscles made freeful retraction necessary and often resulted in some difficulty with proper exposure and in wounds which were more and uncomfortable. Fortunately this problem ceased to exist with the advent of the use of curare-like preparation. In recent years patients who were considered unsuitable for spinal anesthesia have been operated upon under intravenous Pentothal



## SYMPATHETIC DENERVATION OF THE EXTREMITIES; OPERATIVE TECHNIQUE, MORBIDITY AND MORTALITY

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SINCE the introduction of sympathetomy twenty four years ago, the procedure of operative denervation of the sympathetic pathways to the extremities has proved of increasing usefulness in various vascular, hyperhidrotic, and painful disorders. Up to the present time there is nothing to suggest that any means, other than appropriate operations upon the ganglionated chain, are available or are likely to be discovered by which one might hope to achieve permanent interruption of the vasoconstrictor and sudorific impulses, and of the afferent sympathetic pathways, if such exist, without producing at the same time needless loss of somatic nerve function.

The search has continued for various medicinal agents and mechanical devices which might induce sympathetic paralysis and vasodilatation. There can be no doubt that transient vasodilatation can be effected by anesthesia of the sympathetic nerves or of the somatic sensory nerves supplying the area involved by deep general anesthesia and, in the lower extremities, by spinal anesthesia. It is also true that one can ordinarily obtain reflex vasodilatation by heating the body or other extremities, by the intra-arterial, intravenous, intramuscular or subcutaneous injection of certain drugs, and to a lesser extent by ingestion of certain other agent. None of these methods, however, brings about permanent vasodilatation or cessation of sympathetic function. Alcohol injection of the sympathetic pathway results in prolonged sympathetic anesthesia but has the disadvantage that its use is often followed by a distressing neuritis. To be sure, there are certain conditions for which temporary abolition of sympathetic function on one or several occasions is sufficient to yield an immunitely satisfactory result. It would appear evident, however, that operative sympathetomy is the procedure of choice whenever it is advantageous to abolish permanently sympathetic function in an extremity.

It has seemed to me desirable therefore to inquire into the procedure from the standpoint of the ease of its proper execution and the risk attendant upon it. This inquiry would appear to be particularly desirable because although the result of sympathetomy can be so retold so fully accurately in most instances by sympathetic procaine block or by other tests which eliminate vasoconstrictor impulses, there are instances in which the effect of the procedure cannot be predicted with accuracy before operation. Among these exceptions are cases of obliterative arterial disease in which sympathetic blocks or similar tests demonstrat little or no improvement in circulation, certain

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and the peritoneum in the position than they are more medially and less likelihood of inadvertently tearing the peritoneum. The opening is enlarged by introducing into it and separating the two index fingers, and at the same time the peritoneum is pushed away. Blunt dissection with the fingers easily strips the peritoneum from the posterior flank and retroperitoneal tumors. No retractors are used during this procedure. It is wise to stay close to the peritoneum otherwise one may strip off with it a thick layer of retroperitoneal fat and may inadvertently begin dissecting posterior to, rather than anterior to, the diaphragm muscle. The fingers readily pass over the diaphragm muscle to the vertebral bodies. Almost invariably at this point one can identify by palpation the sympathetic chain which is felt as a fixed cord of annulations running along the anterolateral aspect of the vertebral bodies. This exercise should be practiced routinely since useless and troublesome traction can be avoided by experience in locating the chain by palpation, especially in individuals with much retroperitoneal fat or with enlarged aortic lymph nodes.

A broad Deaver retractor is introduced in the mesial portion of the wound. The areolar tissue passing from the vena cava or aorta to the vertebral bodies is incised and is lifted away from the vertebral bodies with the closed blades of a scissor. The retractor is reintroduced and the point of its blade is kept firmly against the vertebral body, then gently pulling the vena cava or aorta medially and exposing the sympathetic chain. A narrow Deaver retractor is used for cephalad retraction and its blade is also kept snugly against the vertebral bodies. No lateral retraction is required except in the rare case in which a long kidney falls into the field of operation. The exposure is now ordinarily excellent. The sympathetic chain is seen running along the anterolateral aspect of the vertebral bodies. The genitofemoral nerve is seen lying on the diaphragm muscle. The ureter is visualized along the peritoneum and is held mesially out of the way by the retractors (Fig. 1). The lower pole of the kidney is seen and fits in the upper outer portion of the wound. The chain is picked up with long smooth forceps between two ganglia and a strand of silk is passed around it with an aneurysm needle. Traction upon this silk lifts the chain off the vertebral bodies. The rami communicantes are readily seen and are divided. In brief performing the operation it is perhaps safe to isolate each ramus separately with a blunt nerve hook before dividing it but after one experience it may be unnecessary. The chain can be safely and quickly divided by passing underneath the ganglia in the direction of the chain a curved scissor, the blades of which are held lightly opened. Before severing the rami one must inspect the area carefully to determine the location of the lumbar veins. With the exception of one small vein which generally crosses anterior to the chain in the region of the fourth lumbar ganglion the veins generally lie posterior to the chain. When they cross anteriorly the veins must be divided between ligatures or clips. Preferably the chain must be secured at its lower end and slipped upward beneath the veins.

In inexperienced hands the entire chain of lymph nodes is severed and from the diaphragm muscle to the vertebral bodies have been mistaken for the

Sodium anesthesia and nitrous oxide or cyclopropane anesthesia after induction with penthal. Curare administered just before the skin incision is made renders the operation as simple and free of trauma as does spinal anesthesia. In this series general anesthesia has been used for twenty-nine operations upon twenty-four patients; in the remainder spinal anesthesia has been employed.

When a unilateral sympathectomy is to be performed the patient is placed upon his back with the side to be explored tilted forward by means of a sandbag so that it is elevated 10 to 20 degrees from the table top. The lower extremity is placed upon a pillow so that the thigh is slightly flexed and the leg muscles relaxed. If a bilateral sympathectomy is to be carried out the patient is placed flat on his back with the thighs slightly flexed. The table is then tilted so as to elevate one side of the body for the first operation, and then the other for the second.

The incision is made from a point on the tip of the twelfth rib downward in a direction roughly following the course of the fibers of the external oblique muscle. In general it is directed toward a point at the junction of the inner and middle thirds of a line drawn from the umbilicus to the anterior superior spine of the ilium. A long incision is not necessary and adds little or nothing to the ultimate exposure, which is necessarily limited by the length of the internal oblique muscle. Generally the skin incision is from 8 to 10 cm. in length. Skin flaps are not dissected back widely from the underlying structures but are freed just sufficiently to permit one to outline clearly the course of the external oblique muscle. The external oblique fascia is incised in the medial portion of the wound and the muscle is split in the direction of its fibers back to the outer margin of the wound. This procedure is facilitated by elevating the margins of the incised fascia by traction upon hemostats which are clamped upon the two edges, by passing the blunt end of a scalpel under the muscle to separate it from the underlying internal oblique and by continuing gentle traction upon the hemostats in such a way as to define clearly the course of the muscle fibers which are quickly and easily separated by incision through the fascial covering from within out and backward. Occasionally a single blood vessel is transected and is clamped and ligated.

Often no bleeding occurs. A small or medium popliteal retractor is then placed in the wound to retract the upper inner portion of the incised external oblique thus exposing the internal oblique up to the point of fusion with the rectus sheath. The fibers of the internal oblique are incised along the course of its fibers from this point downward and posteriorly. The muscle fibers are separated in traction in opposite direction with the dex fingers. At the same time the muscle is freed from transversalis beneath. The retractor is reintroduced so that this layer is brought into view. Occasionally a bleeding vessel will be seen; it must be clamped and ligated carefully so that the intercostal nerve which follows the vessel closely is not included in the ligature. The fibers of the transversalis are spread apart in introducing and opening the blades of a Kelly clamp. This initial opening should be made as far lateralward as is possible since there is less intimate contact between the transversalis

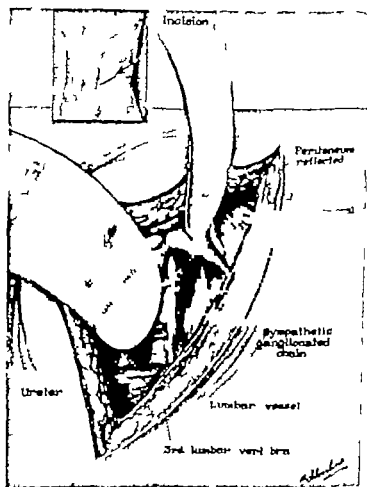
of the chain containing the second and third ganglia can be determined satisfactorily. The chain is more readily exposed on the left side than the right since the vena cava overlies the chain more completely than does the aorta. If the chain is covered by enlarged lymph nodes these may have to be removed in part in order to facilitate exposure. I have seen no harm result. Since the nodes are often traumatized by the dissection even if they are not excised, it is my policy to place sulfanilamide powder or penicillin solution in the wound unless antibiotics or chemotherapeutic agents are to be used parenterally or orally, particularly if there has been any infection of the extremity. This practice holds for dorsal as well as for lumbar operations.

In women it is my custom to remove the first, second, and third or the first, second, third and fourth ganglia. In men the first ganglia are never excised bilaterally unless this procedure seems particularly necessary and the patient has given permission with the understanding that interference with ejaculation may result. No patient has complained of such difficulty after removal of one first lumbar ganglion. In some patients the fourth ganglion has been removed; in others it has been left intact. Thus far I have seen nothing to suggest that its removal has an advantage over its retention, or vice versa. Sometimes the cut ends of the chain have been ligated or clipped with a silver clip; in many this step has been omitted. Once the chain is removed the wound is inspected in order to be sure of hemostasis, the retractors are withdrawn, and the three muscle layers are closed separately with interrupted sutures of silk. The skin is closed with interrupted cutaneous or subcuticular sutures of silk. I have not found it necessary to use lighted retractors. With a little experience the operating room personnel are able to focus the overhead light in such a way as to give satisfactory illumination.

There seems to be a common feeling that the anterior muscle-splitting approach is inadequate for exposure of the first ganglion. I have not found this to be true. Whenever it has been my purpose to include the first ganglion in the resection it has been accomplished without difficulty. Indeed, in one patient I split the diaphragmatic crura and removed the twelfth dorsal ganglion with relative ease (Fig. 9). To be sure this procedure was carried out in a fairly small and thin person but it emphasizes, I believe, the adequacy of the exposure of the upper portion of the lumbar chain.

*Sympathetic Denervation of the Upper Extremity*.—Once stellate gangliectomy proved to be an unsatisfactory method for producing lasting sympathetic denervation of the upper extremity various portions of the upper dorsal and lower cervical chain were resected. It soon became apparent that the stellate and first thoracic ganglion could be left intact and that removal of or decentralization of the upper dorsal ganglia below the level of the first brought about sympathetic paralysis to the upper extremity and half of the head without the production of a Horner's syndrome. In 1937 Telford described an operation in which the second and third thoracic ganglia were decentralized by division of their own communicantes and section of the chain between the third and fourth ganglia. Smithwick in

sympathetic chain. This has not occurred in the series being reported. The chain and the ganglia vary greatly in size but should always be identified with certainty from the characteristic position and course of the chain, and especially from the telltale presence of the rami communicantes. In identifying the respective ganglia two points have proved particularly useful



The fourth ganglion is invariably situated just above the promontory and the first always lies in the region of the lowermost margin of the attachment of the diaphragmatic crura to the vertebral bodies. The second and third ganglia vary considerably in size, shape and position and indeed are sometimes fused. Since the first and fourth ganglia are readily identified, however, that portion

this approach has a its basis the muscle-splitting incision which Hlead and subsequently Hligger had used in performing upper posterior thoracoplasty. The posterior route for exposure of the sympathetic chain after resection of a portion of one rib and its transverse process is based upon the anatomic dissections of Hlerry. From such studies he described in 19— an operation by which the lower cervical and upper dorsal sympathetic ganglia could be reached extrapleurally after the removal of a portion of the second rib and its transverse process.

Early in this experience more or less routinely intravenous Pentothal sodium anesthesia was used without tracheal intubation. Thirty-eight operations upon twenty three patients were performed under Pentothal sodium anesthesia. Although no difficulties were encountered with this method it has been largely replaced by intratracheal cyclopropane or gas-oxygen-ether anesthesia. Since the patients are placed in the ventral decubitus position it is felt that tracheal intubation adds an element of safety. The anesthesia need not be deep during most of the procedure. Even, easy respirations must however be maintained during the period of extrapleural dissection otherwise the hazard of perforating the pleura is increased.

The patient is placed upon the abdomen with the head turned to one side and with the upper extremities alongside the body. A small pillow is placed longitudinally under the thorax so that the scapulae fall away from the midline. The head of the table is elevated about 4 degrees. The skin incision extends from the point between the first and second dorsal vertebral spaces to the spine of the scapula (Fig. 3). The numerous cutaneous and subcutaneous bleeders are clamped. The trapezius is split in the direction of its fibers and is retracted to expose the underlying rhomboid muscles. These are split in the direction of their fibers. Generally this procedure usually involves complete separation of the rhomboid major and minor muscles. Underneath the lowermost fibers of the posterior upper serratus muscle a green The lateral fascial fascia is attached to the inferior margin of the muscle. The fascia is incised all the way at this point and the serratus is retracted superiorly. The lateral portion of the deep muscles of the back are elevated from the third transverse process and are retracted medially with a thyroid retractor (Fig. 4). Great care must be exercised in identifying the third rib. This is usually done without difficulty by passing a finger cephalad between the rhomboid and the serratus, by palpating the uppermost rib and counting superiorly ribs downward. The incision is made through the periosteum of the third rib (Fig. 5) approximately 4 or 5 cm. The periosteum is stripped from the rib and the muscular attachments of the transverse process are carefully lifted so that the entire transverse process is freed. The inner segment of the rib is then exposed and the transverse process is removed. By using a large rongeur it is generally possible to remove not only the entire transverse process with one bite. In stripping the periosteum from the rib and freeing from the rib the underlying intercostal vessels and nerves must be carefully freed from the pleura. Such an accident is not likely to occur if the incision is begun near the

1936 described similar experiences with decentralization of the second and third ganglia. He had obtained the procedure first with resection of a small segment of the second and third intercostal nerves, had subsequently included resection of the corresponding spinal ganglia with extradural section of the roots, and had finally performed intradural root section. In 1940 he<sup>12</sup> described his further experiences with section of the roots through their intradural segments and added as an additional precaution the encasement of the decentralized chain in a silk cylinder. Decentralization rather than excision of the ganglia was practiced in order to render the sympathetic innervation preganglionic rather than postganglionic. The other measures such as removal of the second and third spinal ganglia and a segment of the two intercostal nerves, the intradural section of the roots, and the use of the silk cylinder were aimed at avoidance of postoperative regeneration. These contributions are of fundamental importance.

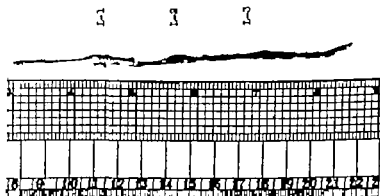


Fig. 2.—Photograph of sympathetic chain, chest through anterior muscle-splitting extraperitoneal incision. In this instance the sympathetic trunks are split and the thoracic dorsal as well as the lumbar chains are excised.

In doing this their original operation of resection of the upper thoracic ganglia. Whit, Smithwick, Allen, and Mixer had located a oblique muscle-splitting approach. They felt that a paravertebral nerve with division of a portion of the trapezius muscle was troublesome from the standpoint of bleeding and often rendered healing difficult. Telford<sup>13</sup> used an anterior approach in decent living the upper dorsal ganglia having given up the posterior approach as too mutilating. When Smithwick first described his preganglionic operation he inverted the paravertebral incision and has continued to use this approach. The operation which I have used is fundamentally the preganglionic operation of Smithwick with intradural section of the anterior roots and in recent years, with encasement of the decentralized chain in a cylinder of fine China silk or nylon. This approach is with slight modification the muscle-splitting operation of Whit, Smithwick, Allen, and Mixer.

a ribral hole where the pleura is less intimately associated with the rib than it is more laterally. The safest method of pushing the pleura away is to slip one's finger beneath the rib and develop the extrapleural space by gentle blunt dissection before the rib is excised. Should the pleura be torn the lung is kept inflated by positive pressure. This accident is troublesome in that the passage of air into and from the pleural cavity may cause any blood in the wound to foam and thus tend to interfere with proper visualization. It adds little or no risk to the procedure. At the end of the operation the lungs are properly inflated as the wound is closed and no effort is made to repair the pleural perforation.

Once the rib and transverse process are excised, the third intercostal nerve is seen lying upon the endothoracic fascia and pleura just above the upper margin of the fourth rib. It is picked up, separated from the underlying tissues and the adjacent intercostal vessels, and a strand of silk is turned around it by means of an aneurysm needle (Fig. 5). The nerve is then ligated laterally, divided, and traced centrally until the spinal ganglion is visualized. The outermost rami communicantes are severed. Next the posterior branch of the spinal ganglion is isolated and divided. The division of this branch is the key to proper mobilization of the spinal ganglion and its roots, for this branch passes directly into the deep muscles of the back and firmly fixes the ganglion centrally. Once it is severed the ganglion can readily be elevated so as to expose the remaining rami communicantes and the dorsal and anterior roots. The rami are divided with a small scissor. A blunt nerve hook is passed between the two roots and by gentle traction the dorsal root is elevated into view. This is then divided by cutting down with a small scalpel upon the nerve hook with which the root is elevated. The same maneuver is useful in dividing the posterior branch of the nerve. If now attempts to sever this branch and the posterior root with scissors one is apt to divide small neighboring vessels from which troublesome bleeding may occur. Once the rami and the dorsal root are divided the only remaining structure connected with the ganglion is the anterior root. If one pulls gently upon the nerve the anterior root can be freed toward the foramen, and with a little additional traction it will be seen to give as a portion of its intradural segment is pulled outside the dura. The intradural portion is readily recognized because of its characteristic glistening white appearance. The root is held by the forceps. Not infrequently there is a leak of spinal fluid as the root is pulled out of the dorsal sac. One should have ready a small bit of firm foam or other hemostatic agent which can be held in the foramen for a few moments. This procedure quickly stops the leak of spinal fluid and without it one at times has great difficulty in closing the back before a number of cerebrospinal fluid have been lost.

The second intercostal nerve is less readily identified than the third as it lies underneath the lower border of the second rib. The pleura should be carefully separated from this rib. One can then generally palpate the nerve with one's finger and with an aneurysm needle separate it from its



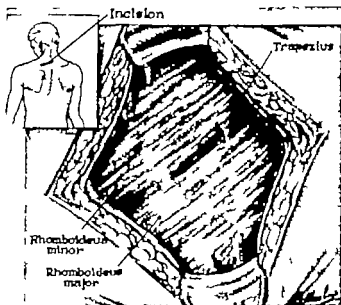


Fig. 2.—Dorsal sympathectomy showing the position of the patient, the line of incision, and the point of separation of the rhomboids. The trapezius has been split in the direction of its fibers and retracted.

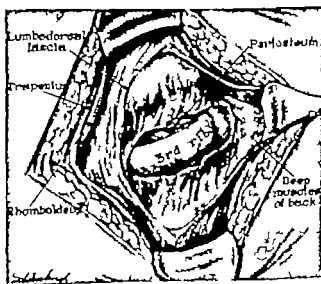


Fig. 3.—View of the third rib cage in order to separate the third rib.

passed about it by means of an aneurysm needle. The chain is then freed from all attachment from a level between the first and second sympathetic ganglia down to a level below the third. The chain is clamped between the third and fourth ganglia, ligated distally and divided. The distal end of the proximal portion of the severed chain is ligated, the silk cylinder is passed over it and ligated gently at its upper end about the chain cephalad to the second ganglion. This ligature must be just tight enough to prevent the sheath slipping down beyond the second ganglion and not tight enough to traumatize the chain. The other end of the cylinder is ligated firmly about the distal end of the freed chain which is then sutured to the longitudinal muscles of the back, or to the

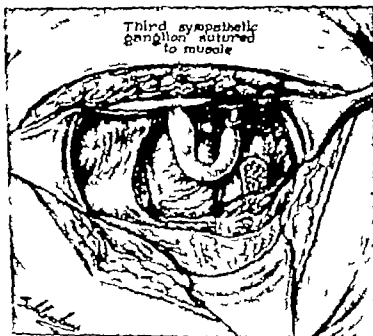


Fig. 4.—Third sympathetic ganglion. The distal end of chain has been covered with silk cylinder and sutured to the muscle.

rhomboids, to leave it out of its normal position. The fascia, the rhomboids, the trapezius, and the superficial fascia are then closed with interrupted silk sutures. The skin is approximated with interrupted subcuticular or cutaneous suture. During closure a small catheter is kept in the extrapleural space. It is withdrawn after aspiration of any fluid or air which may have been present.

The operation for sympathetic denervation of the upper extremity is not a real radical sympathectomy. It is at best a sympathetic gangliotomy. It is not that a sympathetic ganglion is completely removed, but that the sympathetic chain is interrupted. In initial attempts at dorsal sympathectomy, although the technique is not completely radical, nevertheless not particularly difficult and after some experience there is

neighboring vessels, divide it laterally and free it down to the dorsal ganglion. The rami communicantes, the dorsal branch, and the root are now divided. The pleura is separated further from the vertebral bodies until the sympathetic chain can be isolated. Sometimes the chain will be found lying on the pleura, having been dissected off the vertebral bodies. Not infrequently it will have come into view during resection of the dorsal ganglia and the intercostal nerves. When it is first seen, an identifying strand of silk should be

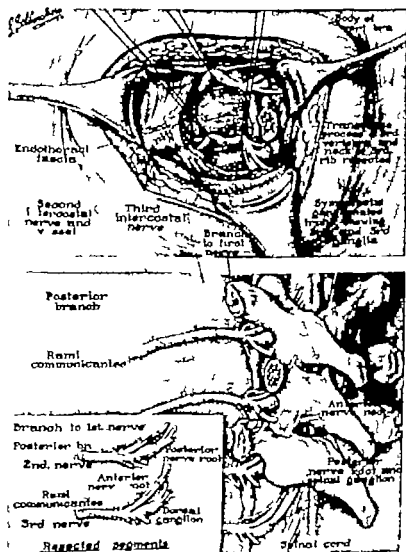


Fig. 8.—Dorsal sympathectomy. The third rib is removed; process has been resected. The intercostal nerve, dorsal ganglia, and the sympathetic chain are exposed. Traction is applied to the posterior branches. At the dorsal ganglia, secondly.

TABLE I DISTRIBUTION OF CASES WITH REGARD TO EXTREMITIES DENERVATED

N. OF EXTREMITIES DENERVATED	NO. OF PATIENTS OPERATED UPON	NO. OF LUMBAR SYMPATHECTOMIES	N. OF DORSAL SYMPATHECTOMIES	N. OF DORSAL AND LUMBAR SYMPATHECTOMIES
One lower	344	344		
Both lower	1-1	1*		
One upper	116		116	
Both upper	27		66	
One upper and both lower		4		
One lower and both upper	6	6	10	
All four		1	12	
Total	627	667	206	12

dorsal sympathectomies were done transpleurally the remaining 200 dorsal sympathectomies were performed essentially as I have described this operation. In the earliest cases the anterior root section was extradural in the others the anterior root was sectioned through its intradural portion. In the past four years the centralized chain has been encased in a silk or nylon cylinder. No stellate gangliectomies are included in this study and no cases of lumbodorsal sympathectomy with aplanchnic resection.

During the period covered by this survey there was failure to accomplish a satisfactory denervation in 4 cases, in addition to the successful completion of the procedure in 613. In one case an inexperienced operator working without supervision, had difficulty in exposing the lumbar chain and abandoned the procedure. A bilateral sympathectomy was accomplished without difficulty a few weeks later. In one patient the operator had finished a unilateral lumbar sympathectomy upon the involved side and was proceeding with the other side when he found the spinal anesthesia was no longer effective. The patient had obliterative arterial disease with symptoms limited to one extremity the other was being denervated simply to provide the patient with what safer continued vasodilatation might give him. Rather than give the patient a general anesthesia it was decided to defer the second gangliectomy. Once before adequate experience with dorsal sympathectomy had been obtained the procedure was abandoned in a man of extraordinarily heavy build in whom a pleural tear had been made and in whom proper exposure was difficult. The patient was operated upon successfully at a later date. Only once has an experienced operator failed to achieve the sympathetic denervation he desired to carry out. This was the case of an unrecognized resection of the fourth instead of the third rib with consequent decentralization of the third and fourth rather than of the second and third dorsal sympathetic ganglia.

The sympathectomies were performed at many occasions. In Table II the primary indications for operation are listed together with the final results. In segregating the patients into the different groups man had to be placed arbitrarily in one group or another since several characteristics were exhibited by a single patient. In some patients there was major caudalgia,

rarely any trouble with its proper execution. The operation must be done in a bloodless field. The area in which the nerves are exposed is necessarily small and good visibility is essential. Overhead lights are satisfactory. Great care must be taken to avoid pleural perforation as this complication increases the difficulty of exposure and dissection. Of extreme importance is the proper identification of the third rib. This rib can generally be identified with ease by counting the uppermost ribs while palpating between the rhomboid and serratus muscle layers. If any doubt whatsoever exists, it is my practice to check further the identity of the rib after its resection by gently pushing the pleura away from the superior ribs and counting them by palpation from their undersurface. By this maneuver one can be certain of the location of the first rib since the subclavian artery is always palpable at its upper margin. If there is doubt as to the location of the third rib beforehand the uppermost of the ribs in question should be resected. One can perform the operation adequately through resection of the second rib, though the third sympathetic ganglion is isolated with more difficulty with the second rib removed than the second ganglion with the third rib removed, and the third root section cannot be performed properly with this exposure. When the fourth rib is mistakenly excised, on the other hand, it is impossible to accomplish a satisfactory denervation of the upper extremity. Should the mistake be recognized one should proceed with resection of the third rib as well. Resection of two ribs instead of one is a thought which not infrequently occurs to the inexperienced operator who is finding adequate exposure somewhat difficult to achieve. Any gain in the area of exposure is, however, lost in the increased pleural motion in the field and in the additional hazard of pleural perforation.

#### CLINICAL MATERIAL

This study is based upon a survey of operative sympathetic denervation of 813 extremities in 627 patients. Six hundred thirty-seven of these operations were performed by me or under my direction at the New Haven Hospital, the Johns Hopkins Hospital, and at various army installations. This group included about 83 per cent of the dorsal and 77 per cent of the lumbar sympathectomies analyzed. The remaining 17 operations were performed by others at the Johns Hopkins Hospital between October 1939 and October 1946.

Unilateral lumbar sympathectomies were performed upon 344 patients, bilateral lumbar sympathectomies upon 11, unilateral dorsal sympathectomies upon 116, and bilateral dorsal sympathectomies upon 33 (Table I). In addition, 2 patients underwent unilateral dorsal and bilateral lumbar sympathectomy, 5 had bilateral dorsal and unilateral lumbar sympathectomy and in 8 all four extremities were denervated. Fifty-four bilateral lumbar sympathectomies were carried out in one stage. In only four cases was a bilateral dorsal sympathectomy performed in one session.

Altogether there were 607 lumbar sympathectomies. In no case a bilateral ganglionectomy was performed through a transperitoneal approach. All the remainder were done essentially in the manner which I have outlined. Four

TABLE I. DISTRIBUTION OF CASES WITH REGARD TO EXTREMITIES DENERVATED

NO. OF EXTREMITIES DENERVED	NO. OF PATIENTS OPERATED UPON	NO. OF LUMBAR SYMPATHETIC TOMIES	NO. OF DORSAL SYMPATHETIC TOMIES	% OF DORSAL AND LUMBAR SYMPATHETIC TOMIES
One lower	54	54		
Both lower	11	22		
One upper	116		116	
Both upper	31		61	
One upper and both lower		4		
One lower and both upper	8	8	10	
All four		1	1	
Total	220	107	176	913

dorsal sympathetomies were done transpleurally the remaining 20 dorsal sympathetomies were performed essentially as I have described this operation. In the earliest cases the anterior root section was extralaminar in the others the anterior root was sectioned through its intradural portion. In the past four years the decentralized chain has been crossed in a silk or nylon cylinder. No stellate ganglionectomies are included in this study and no cases of lumbar dorsal sympathectomy with splanchnic resection.

During the period covered by this survey there was failure to accomplish a satisfactory denervation in 4 cases, in addition to the successful completion of the procedure in 813. In one case an inexperienced operator working without supervision had difficulty in exposing the lumbar chain and abandoned the procedure; a unilateral sympathetomy was accomplished without difficulty a few weeks later. In one patient the operator had finished a unilateral lumbar sympathetomy upon the involved side and was proceeding with the other side when he found the spinal anesthesia was no longer effective. The patient had obstructive arterial disease with symptoms limited to one extremity; the other was being denervated simply to provide the patient with what safety continued vasodilatation might give him. Rather than give the patient a general anesthesia it was decided to defer the second ganglionectomy. Once best adequate experience with dorsal sympathetomy had been obtained, the procedure was abandoned in a man of extraordinarily heart build in whom a pleural tear had been made and in whom proper exposure was difficult. The patient was operated upon successfully at a later date. Only once has an experienced operator failed to achieve the sympathetic denervation he desired to carry out. This was the case of an unrecognized resection of the fourth instead of the third rib with consequent decentralization of the third and fourth rather than of the second and third dorsal sympathetic ganglia.

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Unilateral lumbar sympathectomies were performed upon 344 patients, bilateral lumbar sympathectomies upon 121, unilateral dorsal sympathectomies upon 116, and bilateral dorsal sympathectomies upon 33 (Table I). In addition, patients underwent unilateral dorsal and bilateral lumbar sympathectomy, 5 had bilateral dorsal and unilateral lumbar sympathectomy and in 6 all four extremities were denervated. Fifty-four bilateral lumbar sympathectomies were carried out in one stage. Only four cases were a bilateral dorsal sympathectomy performed in one session.

Altogether there were 607 lumbar sympathectomies. One case of bilateral ganglionectomy was performed through a transperitoneal approach. All the remainder were done essentially in the manner which I have outlined. Four

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One lower	344	344		
Both lower	11	22		
One upper	116		116	
Both upper	53		66	
One upper and both lower		4		
One lower and both upper	5	5	10	
All four	8	1	1	
Total	627	607	206	813

dorsal sympathetomies were done transpleurally the remaining 202 dorsal sympathetomies were performed essentially as I have described this operation. In the earliest cases the anterior root section was extradural in the thorax the anterior root was sectioned through its intradural portion. In the past four years the decentralized chain has been encased in a silk or nylon cylinder. No stellate gangliotomies are included in this study and no cases of lumbodorsal sympathetomy with splanchnic resection.

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reduction in circulation from ligation of a major artery following trauma, and neurilemmic paralyses of nerves. Patients undergoing lumbar sympathectomy averaged 36 years in age with a range from 16 to 80; those undergoing dorsal sympathectomy averaged 25.6 years in age with a range from 18 to 60. Only 18 of the 167 patients who had dorsal sympathectomy and in whom the exact age is known were 40 years of age or more (Table III). One hundred sixty-three of the 423 patients who underwent lumbar sympathectomy and upon whom the exact age is known were 40 years of age or older and 10% of them were 60 or older. Six of the 25 patients in whom the exact age is not available were in the older age group. Hence approximately 17 per cent of those subjected to lumbar sympathectomy were 40 years of age or older.

TABLE III. AGE DISTRIBUTION OF PATIENTS UPON WHOM REMEDIAL SYMPLECTOMY WAS PERFORMED

AGE OF PATIENTS (Y)	AGE (X OF PATIENTS)	NUMBER OF PATIENTS
Less than 20	16	1
20 to 30	24	13
30 to 40	37	116
40 to 50	1	4
50 to 60	2	3
60 to 70	2	27
70 to 80	0	15
80 or more	0	1
Age not known	3	25
Total	16	174

The majority of all the patients were in excellent general health. Many in the younger age group were soldiers in the best possible condition; a fairly large number, however, were debilitated by long-continued illness. Many of the patients with peripheral arteriosclerosis had generalized cardiovascular disease and many had diabetes and hypertension. A few of the patients were very poor operative risk. In addition to such disorders as diabetes, hypertension, and generalized vascular disease, not a few had severe cardiac disease with marginal or poor compensation, auricular fibrillation, or recent myocardial infarction. A few patients in whom sympathectomy might otherwise have been performed were not operated upon because of such diseases as severe recent myocardial infarction or pneumonia. That the patients did not generally constitute a selected group is perhaps indicated, however, by the fact that I have performed only two lumbar sympathectomies since the beginning of the period covered in this survey.

#### POSTOPERATIVE COURSE AND COMPLICATIONS

In general the patients stood the operation extraordinarily well and had comfortable convalescence and a short period of hospitalization. When bilateral sympathectomies were performed at the same time the operations were usually spaced from five to eight days apart. Nearly all patients took a regular diet the evening of the day of operation or the following day. Distention, nausea, and constipation occurred exceedingly seldom. All of these patients in whom

TABLE II. INDICATIONS FOR OPERATION

INDICATION FOR OPERATION	ON 14 SEP. (RECTIONS)				ON 14 SEP. (RECTIONS)				ON 14 SEP. (RECTIONS)			
	OPER. TIME	AGE (YR.)	PRE-AGE	OPERATION	TIME	AGE (YR.)	PRE-AGE	OPERATION	TIME	AGE (YR.)	PRE-AGE	OPERATION
Hayward's disease	16	40-47	11-4	44	44	1-14	11-7	47	44	1-14	11-7	47
Raynaud-like disorders, hyperhidrosis, etc.	29	1-11	49-7	46	8	-2	47	47	46	8	47	47
Trench foot	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Frostbite	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Charcot's and phalangeal bone pain	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Posttraumatic sensory disorders	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Paralysis of the peroneal leg fibers, etc.	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Traumatic thermal injury with ligature or thrombosis	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Aneurysms and arteriovenous fistula	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Arterial embolism or thrombosis	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Thromboangiitis obliterans	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Arteriovenous and diabetic ulcers	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Tenodesis	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46
Total	44	1-7	40-3	46	46	1-7	40-3	46	46	1-7	40-3	46

In six patients a minor wound infection occurred, either one or more stitch abscesses, or a small abscess. No difficulty or prolongation of hospitalization resulted. There was only one serious wound infection. This was the case of a patient with Raynaud's disease who developed after dorsal sympathectomy an infection involving all portions of the operative incision. The infection subsided after the wound was opened and drainage was established. In two patients there was a partial separation of the skin edges, prompt healing without infection occurred. One patient with a peculiar disorder characterized by Raynaud's phenomenon in all four extremities and by unexplained areas of necrosis of the skin developed another area of necrosis just caudal to the operative incision. In this instance a dorsal sympathectomy had been performed transthoracically through an anterior incision.

Altogether wound complications were recorded in fifteen cases, an incidence of 1.8 per cent. It is possible that trivial stitch abscesses or small hematomas may have gone unrecognized in a few, or that such observations were not recorded. In general however members of the staff who cared for these patients were alert and careful to make notes of such complications. At any rate it is evident that more or less serious complications were limited to four patients, two with hematomas, one with a serious infection, and one with a necrotic ulcer near the incision.

In nine patients there was evidence suggestive of hemothorax or pneumothorax. All of these patients did well with the usual therapeutic measures and in none was hospitalization prolonged. A spontaneous bilateral pneumothorax occurred in one patient after a right dorsal sympathectomy. In this case the pleura was not perforated at operation. As the procedure was being terminated a small amount of air was noted under the pleura. Not only was it seen in the pleural space but there was no sucking in or blowing out of air with respiratory movements or of the saline solution used for irrigation. Within a few minutes after completion of the operation a tension pneumothorax was present. A thoracentesis with removal of the air and re-establishment of normal intrapleural pressure gave relief from the dyspnea and cyanosis. A short while later the patient was again dyspneic and cyanotic and had signs of a pneumothorax on the opposite side. Again relief was obtained from thoracentesis and a portion of a lung recurrence took place and roentgenograms taken the following day revealed no residual pneumothorax on either side. Though no definite emphysematous blebs were visible in the roentgenograms, it was felt that breaking of such blebs in all likelihood accounted for this unusual difficulty. In another patient an uncomplicated dorsal sympathectomy executed without pleural perforation was followed by an unexplained serious pleural effusion which increased in extent over a period of several days and required several thoracenteses before it finally disappeared. One patient developed a small hemothorax after each of two dorsal sympathectomies. In each instance the pleura was torn during the dissection. No difficulty resulted. Another patient developed a massive serousopurulent effusion after a dorsal sympathectomy during which the pleura was torn. A single thoracentesis with removal of almost all

no specific contraindication existed were made ambulatory early during the past six years nearly all such patients were out of bed and walking the day after operation. Unless some local lesion such as ulceration or some general condition such as heart disease made prolonged hospitalization necessary most of the patients were discharged in from four to eight days after operation.

In Table IV are listed the complications which occurred. There were three hematomas of wounds. Several hours after completion of a lumbar sympathectomy one patient complained of pain in the wound, inspection of which revealed a hematoma rapidly increasing in size. The wound was explored and a small arterial bleeder was found in the internal oblique muscle. This was ligated, the wound re-sutured, and no further difficulty ensued. In another individual the wound developed in the retroperitoneal space a moderate-sized deep hematoma which caused discomfort for a few days but which subsided satisfactorily without specific treatment. A third patient developed a small hematoma after dorsal sympathectomy; no treatment was required. Two additional patients developed a serous effusion in the wound after dorsal sympathectomy; in both instances bacterial cultures were negative and the effusion did not recur after one or two aspirations.

TABLE IV. COMPLICATION AFTER SYMPLECTOMY

INDICATION FOR OPERATION	NO. OF OPERATIONS	AGE OF PATIENTS (YE)		WOUND COMPLICATIONS							CHEST COMPLICATIONS						
				WOUND HEMATOMA	WOUND INFECTION	WOUND DEBRIDEMENT	WOUND REPAIR	WOUND XI	WOUND XII	OTHER	LOCAL TUBERCULOSIS OR PNEUMONITIS	PNEUMOTHORAX	PULMONARY EMPHYSEMA	PNEUMOTHORAX	PULMONARY EMPHYSEMA		
		RANGE	MEAN														
Lumbar Sympathectomy																	
Vasospastic disorders	47	16-57	29.7	1													
Trench foot and frostbite	89	19-35	27.4														
Arterial injury atherosclerosis, embolism, posttraumatic aneurysms, etc.	124	19-69	37	1	1			1									
Postphlebotic syndrome and leg ulcers	74	17-66	37.0						1								
Obliterative arterial disease acute arterial thrombosis and embolism	44	21-40	40.9			5					5					1	
											5					1	
											1	2		1	1		
											2	1		1			
All Sympathectomies																	
Arterial injury atherosclerosis, embolism, posttraumatic aneurysms, etc.	4	21-50	31.6														
Obliterative arterial disease acute arterial thrombosis and embolism																	
All	506	18-69	37	5	1	1		1			4	1	1	1	1		
All Sympathectomies																	
Total	613	18-50	33.9	5	1	0	1	2	1		0	1	1	1	1		

slight caudal enlargement, calcification of the aortic mural pulmonary embolism, and interstitial fibrosis.

There were no deaths following dorsal sympathectomy. There was only the one death following sympathetic denervation of 607 lower extremities performed in 553 operations upon 478 patients. Considering only those patients 50 years or more in age there was one fatality following 120 operations (166 sympathetic denervation of extremities) upon 11 patients. The operative mortality of unilateral or bilateral lumbar sympathectomy was thus 0.18 per cent for the entire group, and 0.78 per cent for those patients 50 years or more in age.

With regard to complications which may occur during the operative procedure itself, it may be said that these were almost completely limited to inadvertent perforation of the peritoneum or pleura. Tearing into the peritoneal cavity was exceedingly rare even in the hands of inexperienced operators; in all such cases the peritoneal laceration was sutured and the operation completed without difficulty. The incidence of pleural perforation during dorsal sympathectomy was almost in every proportionate to the surgeon's experience with the operation. In general this difficulty occurred often during the early experiences and infrequently once the technique was well mastered.

Two other complications remain to be discussed. One is the occurrence of a spinal headache following dorsal sympathectomy with intradural root section associated with loss of spinal fluid. A few cases of severe headache lasting for from a few days to a week or more occurred in my early experience with intradural root section before it became evident that the leak of spinal fluid could be quickly and efficiently sealed off by holding a plug of fibrin foam against the foramen for a few moments after section of the root. Since this precaution has been taken no headaches have occurred.

The second complication is a distressing discomfort in the thigh which may follow lumbar sympathectomy. The onset of this discomfort is rarely immediate but usually begins from a few days to a week after operation. It generally lasts for only a few weeks but has persisted in a few patients for from six weeks to two months. Sometimes this discomfort is intermittent and is present chiefly at night; sometimes it is more or less constant. The patient finds it difficult to describe the pain accurately or to localize it well. Most of them describe it as a deep aching sensation felt diffusely through the deep tissues of the thigh. It is not associated with cutaneous sensory changes or with any motor alterations but is sometimes associated with slight tenderness of the thigh muscles. Its cause is unknown. Efforts at alleviating the discomfort have not been particularly successful. In some individuals warm tub baths have given more relief than anything else. In some mild sedatives such as acetaminophen and are helpful. In others codeine and demerol have not been very effective. A few particularly those with night pain only appear to be relieved in part but never completely by small doses of quinine. Unfortunately no accurate record of the incidence of this complication has been kept. At one time notes were kept concerning its occurrence in thirty consecutive cases and it

the bloody effusion subsided and convalescence was rapid. In one patient a questionable small pulmonary infarction occurred. There was a sudden onset of chest pain with cough and a pleural rub. Though roentgenograms were indeterminate and there was no evidence of peripheral venous thrombosis, this was felt to be an instance of a small pulmonary embolism.

There were thus recorded fifteen instances of pulmonary complications, an incidence of 1.8 per cent. Again it must be said that it is entirely possible that a few cases of minor pulmonary complications went unrecognized or were not recorded. A careful scrutiny of the records and of the charts of vital signs failed, however to reveal other instances which were particularly suggestive of such difficulties.

Except for the one case of probable pulmonary embolism, there were no other cases in which there was anything to suggest the occurrence of phlebotrombosis or thrombophlebitis. One patient after a lumbar sympathectomy had a febrile course of moderate degree for about one week; no adequate explanation was ever found for the fever. One postoperative death occurred. The case report follows.

#### CASE REPORT

The patient was 68-year old woman with generalized arteriosclerosis, arteriolecular cardiovascular disease, moderate hypertension, and diabetes mellitus. She had been admitted to the hospital on Nov. 24, 1944, with painful and infected area of superficial gangrene involving the right third toe. There were no arterial pulsations palpable in either lower extremity below the groin and the circulation was badly impaired in both feet. She experienced relief of pain during period of sympathetic procaine anesthesia though there was no rise in skin temperature or improvement in color of the foot. No healing appeared to be taking place after an open amputation of the distal phalanx of the infected and gangrenous right third toe. On December 30, right lumbar sympathectomy was performed. The pain dropped and the stump began to heal. On Jan. 15, 1947, cholecystectomy was performed for an acute exacerbation of chronic cholecystitis and cholelithiasis. The toe was well healed at the time of the patient's discharge on February 2. She readmitted few days later with signs of thrombophlebitis in the right lower extremity. She was treated with anticoagulant therapy and discharged in three weeks. She continued to have some dependent edema and on elastic support. In May she began to have severe rest pain at night in the left leg and foot. The pain continued and in July she developed areas of gangrene of the left second and third toes. She was admitted to the hospital on July 14. A left lumbar sympathetic block afforded temporary relief of pain but very little improvement in circulation. In spite of the excellent result which she had obtained in somewhat similar circumstances following right lumbar sympathectomy, it was felt that supracervical amputation was the procedure of choice. The patient refused to have this done, however, and on July 29, left lumbar sympathetic ganglionectomy and amputation of the distal phalanx of the second toe were performed under spinal anesthesia supplemented with intravenous Pentothal Sodium. She appeared to be doing well postoperatively. She had no pain in the left lower extremity; the circulation in the stump appeared slightly improved, and the general condition seemed quite satisfactory. She quite active in bed and took the diet well until the fifth postoperative day when she had a severe attack of pneumonia. Early the next morning she was

this injection had been made. Roentgenograms made one week before operation showed and an amputation was not obtained.

From this study it would appear that the operations for bringing about sympathetic denervation of the upper and lower extremities are useful procedures which cause little discomfort to the patient necessitate only a brief period of hospitalization, are followed by few complications, and carry a small risk of fatality. Both procedures requires a thorough knowledge of the anatomy involved and can be done properly only with precise and gentle dissection. With proper tutelage lumbar ganglionectomy can be mastered fairly early in the course of surgical training. Dorsal sympathectomy should not be attempted by anyone until he has become a fairly adept operator and then only with initial assistance of one experienced in the procedure. Anal-ysis of the fairly large experience reported in this survey would suggest that both dorsal and lumbar sympathectomy are sufficiently safe operations to warrant their application when they appear to offer reasonable promise of improvement in the patient's condition.

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Absence of sweating in the area denervated is an expected physiologic response to sympathectomy. Sometimes this result is the chief aim in sympathectomy as in cases of annoying hyperhidrosis or bromhidrosis. Fortunately in other instances of peripheral vascular disease as well the postoperative absence of sweating is of real benefit to the patient since there is no longer an local evaporation with the consequent increased heat loss and decreased circulation and since maceration of skin and fungus infections are less likely to occur in the dry hand or foot. Rarely does any trouble result from the dryness of skin, provided each patient conscientiously keeps the skin well lubricated with lanolin as he is directed to do. Occasionally patient develops cracks in the skin but this occurrence is generally limited to those who have seasonal climatic alterations and who have been negligent in the care of the skin. Uncommonly there is a noticeable increase in sweating in the normally innervated areas of the body after sympathectomy, especially in persons who tend to sweat profusely with emotional excitement exercise or in hot weather. Only a very few have had such complaints after bilateral lumbar or dorsal sympathectomy or even after three extremities have been denervated. Of the six patients in whom all four limbs were sympathectomized, however there was distressing hyperhidrosis in the normally innervated trunk in three. One indeed was so bothered by this phenomenon that he wondered whether the relief of the Raynaud symptoms was benefit enough to justify the operation. The others felt that the increased sweating of the trunk was of little concern in view of the marked relief which the sympathectomy had afforded. Patients in whom extensive sympathetic denervation is thought desirable should, however be warned of the possible occurrence of increased sweating in the normally innervated portions of the body and sympathectomy should be limited to two or three extremities unless the indications are clear for performing it upon all four.

#### SUMMARY AND CONCLUSIONS

It has been generally assumed, I believe by most of those who are actively engaged in percutaneous work upon the sympathetic nervous system that these procedures are well tolerated by patient and carry little risk. One certainly gets this impression from most of the reported experiences. It is undoubtedly true however that many physicians must look upon sympathetic denervation of the extremities as rather formidable operations otherwise it is difficult to understand their persistence in the use of their less effective means of treatment in cases which appear to profit maximally from sympathectomy. It is also true that some surgeons have hesitated to perform periarterial stripping in lieu of direct attack upon the ganglionated chain because of the supposed risk associated with these procedures. Leriche and his associates,<sup>20</sup> for example have stated that lumbar sympathectomy carries a mortality of 4 per cent or more.



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## THE EARLY EFFECT OF LUMBODORSAL SYMPATHECTOMY UPON THE RESPONSE TO INSULIN IN MAN

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THE sympathicoadrenal system is an integral part of the physiologic organization which maintains the concentration of sugar in the blood within normal limits (Cannon). Using the denervated heart as an index for circulating adrenaline, Cannon, McIver and Bliss<sup>1</sup> observed that when the level of the blood sugar fell to 70 or 80 mg. per cent in unanesthetized cats, there was a demonstrable secretion of adrenaline into the circulation. The liberation of this hormone was prevented by removing one adrenal and denervating the other or by injecting dextrose solution to correct the hypoglycemia. Cannon, McIver and Bliss further noted that when the adrenals were inactivated convulsions occurred with smaller doses of insulin and sooner after its injection than in the control animals. By means of crossed circulation experiments in the dog, Housley, Lewis, and Molinelli<sup>2</sup> demonstrated secretion of adrenaline when insulin induced hypoglycemia reached levels of about 50 mg. per cent. They used the hyperglycemic response to circulating adrenaline as their indicator. They too, showed that sympathetic denervation of the adrenal glands or the injection of glucose solutions intravenously prevented the liberation of adrenaline into the circulation. Burn had already shown in 1923, that the injection of ergotoxine, which was known to paralyze the positive effects of sympathetic nervous system activity made rabbits more sensitive to insulin than normally.

Britton Gelling and Calvery studied the response to insulin in the same animals before and after excision of one adrenal gland and denervation of the other by splanchnicectomy and removal of the upper 1 or 2 cm. of the lumbar sympathetic chain. They found that after operation greater degrees of hypoglycemia and severer reactions to it were obtained even though smaller doses of insulin were used than before excision of the adrenal glands from sympathetic control. While in the preoperative animal convulsions were attended by a rise in the concentration of sugar in the blood, after operation convulsive seizures were followed by a further lowering of the insulin hypoglycemia.

Dworkin confirmed the stimulation of the sympathicoadrenal system by insulin-induced hypoglycemia in the cat and observed that completely sympathetomized cats developed signs of hypoglycemia with much smaller doses of insulin and more quickly than normal animals did after the injections. Schlossberg, Sawve and Bixby<sup>3</sup> pointed out that if doses of no more than 0.5 unit of insulin per kilogram were used, no symptoms developed in the animals and no difference could then be demonstrated in the response to insulin of nor-

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mal and sympathectomized cats. When 0.5 unit of insulin per kilogram of body weight was used, however, obvious differences could be detected between the control and experimental animals. Among the control animals marked symptoms and convulsion occurred in only one out of seven. All of the sympathectomized animals had severe symptoms and three of them had convulsions without spontaneous recovery but requiring the parenteral administration of dextrose. The blood sugar concentration fell to its lowest point more rapidly in the sympathectomized animals than in the normal controls. Schlossberg and associates reported that the blood sugar fell to lower levels in the sympathectomized animals than in the controls, but their figures for this conclusion are not entirely convincing. Freeman, Smithwick, and White<sup>14</sup> observed a similar sensitivity to insulin in the rabbit after denervation of the adrenal glands. In the dog, de Takáts and Cuthbert<sup>15-16</sup> showed both an increased glucose tolerance and an increased insulin sensitivity after denervation of the adrenal glands, and Ciminatti reported that he had counteracted the effects of pancreatectomy in a dog by denervation of the adrenal glands. These data furnish ample evidence for the important role that the sympathoadrenal system plays when the mechanisms which regulate the concentration of sugar in the blood are put under stress.

Tests of the sensitivity of patients to insulin and to hypoglycemia have already found clinical application. In 1941 Fraser, Albright, and Smith presented a composite curve for the response of normal individuals to intravenous insulin. By comparison of the hypoglycemic responses in endocrinopathies with the normal curve obvious differences were demonstrable and the insulin tolerance test was thought to be of value in that it brought out hypoglycemia unresponsive in patients with hyperinsulinism, panhypopituitarism, and hypoadrenocorticism. Meduna and McCulloch<sup>17</sup> illustrated a difference between insulin tolerance curves in normal and in psychiatric patients. More recently Aronson and McCulloch<sup>18</sup> demonstrated differences between normal and oneiroptic patient in the responses to insulin and to insulin hypoglycemia. They pointed out that the difference could be detected as early as fifteen minutes after the injection of insulin and by using doses of 0.1 unit per kilogram of body weight or even with doses as low as 0.01 unit of insulin per kilogram of body weight. In their report on the surgical aspects of hypertension, de Takáts, Herer and Keeton presented evidence of increased sensitivity to insulin after sympathectomy.

In the light of the experiences just reviewed it was thought possible that the responsiveness to insulin and to the ensuing hypoglycemia might be used as a test for completeness of denervation of the adrenal glands and for regeneration of sympathetic nerves in once denervated adrenal gland. Information so obtained would be very useful in the evaluation of the causes for failures in the treatment of hypertension by sympathectomy.

#### METHOD

Patients of both sexes in private and public ward were used in the study. Those who had an evidence of diabetes mellitus were excluded. The patients tested varied in age from 19 to 55 years. The average age was 41 years. The

response of the blood sugar concentration to insulin injected intravenously was tested as part of a series of physiologic tests done both before and after operation. In some patients (twenty-two cases) tests were made in the interval between stages of sympathectomy. The patients had been on a house diet consisting of about 70 Gm of protein, 50 Gm of fat, and 300 Gm of carbohydrate per day for a period of a week or more before the test. Following operation, they had been on a house diet for ten days (average) before the test and were ambulatory. Fraser, Albright, and Smith recommended a diet containing 300 Gm of carbohydrate in each of the three meals preceding the test. This recommendation was not followed in the present study because it was anticipated that difficulty might be experienced in obtaining so high a carbohydrate intake in postoperative patients. The subjects were therefore allowed a house diet without rigid control both before and after operation. Patient who showed any signs of fever on the day preceding the scheduled test were not studied until a later date. The subjects had fasted for twelve to fifteen hours before the test was begun.

The extent of the sympathectomies in the patients studied is represented in Fig. 1. All of the patients had at least a bilateral removal of the ninth to twelfth thoracic ganglia inclusive, and of the major splanchnic nerve. The lesser and least splanchnic nerves were necessarily decentralized and actually excised in most instances. When, in individual cases, the extent of sympathectomy was greater than the minimum of the ninth through the twelfth thoracic ganglia the spread was generally as much above the ninth as it was below the twelfth thoracic. One exception to this general rule was a patient with both hypertension and Raynaud's disease for whom a sympathectomy was done, including the second through the twelfth thoracic ganglia bilaterally. In addition, the denervations extended through the third thoracic in two patients on the right side and in four patients on the left side.

The insulin dosage adopted was 0.08 unit per kilogram of body weight injected intravenously. Pilot test had resulted in symptoms of hypoglycemia and in a drop of the blood sugar level to as low as 49 mg per cent (an actual drop of 40 mg per cent from the fasting) when as little as 0.04 units of insulin per kilogram of body weight were injected intravenously. De Takáts, Heyer and Keeton had obtained useful responses to 0.01 unit of insulin intravenously per kilogram of body weight. Since some patients had shown an inadequate response to 0.04 unit of insulin per kilogram, however, it was decided to use double that amount as the standard test dose. A larger dose was adopted purposely because it was feared that an overwhelming dose of insulin might not discriminate between the normal and sympathectomized patients, such as too large a dose of adrenalin fails to discriminate between the responses of normal and sensitized smooth muscle.

Blood samples were obtained in duplicate shortly before the injection of insulin and approximately 15, 30, 45, and 60 minutes after the injection. Specimens were then obtained every half hour until 3 hours (in some cases 1½ hours) after the injection of insulin. No attempt was made to collect the blood specimens exactly on time but the exact time that each specimen was taken was care-

fully noted to the half minute. For compiling the data, the mean time of the points for each group of determinations was used on the abscissa to correlate the blood sugar level and the time after the injection of insulin. The reducing substances in 0.1 c.c. of capillary blood were measured by the method described by Folin and Malmros. This gives values lower by about 10 mg. per cent than those obtained by the method of Folin and Wu.<sup>12</sup>

# EXTENT OF SYMPATHECTOMY

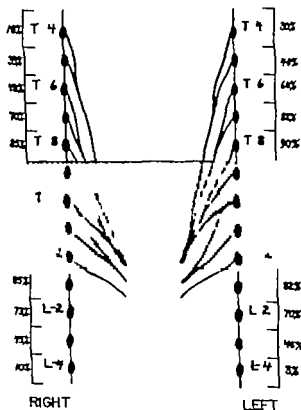


Fig. 1.—The right and left panels show curves of the major, intermediate, and least sympathectomy are represented diagrammatically. The extent of sympathectomy indicated by the letters on both sides represents per cent of the total group of thirty-three patients. The numbers in parentheses represent the percentage of operation for all of the cases.

When the data were assembled they were tested statistically for significance. Standard deviations of individual values from the means were calculated by the formula  $\sigma = \sqrt{\frac{\sum d^2}{N-1}}$  and the standard error of the means was obtained from the formula  $\sigma_m = \frac{\sigma}{\sqrt{N}}$ . The standard error of percentages was tested by the formula  $\text{Standard Error} = \sqrt{\frac{1-P}{N} - \frac{1-P^2}{N}}$  where P is the percent



response of the blood sugar concentration to insulin injected intravenously was tested as part of a series of physiological tests done both before and after operation. In some patients (twenty-two cases) tests were made in the interval between stages of sympathectomy. The patients had been on a house diet consisting of about 70 Gm. of protein, 50 Gm. of fat and 300 Gm. of carbohydrate per day for a period of a week or more before the test. Following operation, they had been on a house diet for ten days (a stage) before the test and were ambulatory. Fraser, Albright, and Smith recommended a diet containing 300 Gm. of carbohydrate in each of the three weeks preceding the test. This recommendation was not followed in the present study because it was anticipated that difficulty might be experienced in obtaining so high a carbohydrate intake in postoperative patients. The subjects were therefore allowed a house diet without rigid control both before and after operation. Patients who showed any signs of fever on the day preceding the scheduled test were not studied until a later date. The subjects had fasted for twelve to fifteen hours before the test was begun.

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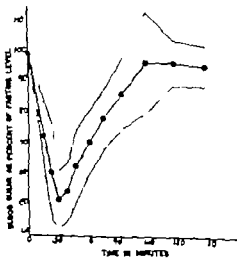
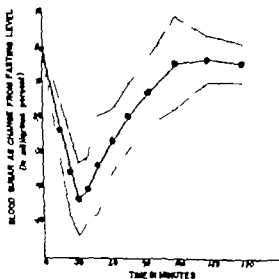
amount as the standard test dose. A larger dose was used possibly because it was feared that an overwhelming dose of insulin might not discriminate between the normal and sympathectomized patients, much as too large a dose of adrenalin fails to discriminate between the responses of normal and sensitized smooth muscle.

Blood samples were obtained in duplicate shortly before the injection of insulin and approximately 15, 30, 45 and 60 minutes after the injection. Specimens were then obtained every half hour until 3 hours (in some cases 2½ hours) after the injection of insulin. No attempt was made to collect the blood specimens exactly on time, but the exact time that each specimen was taken was care-

standard error of individual determinations from that mean is represented by the shaded area above and below the curve. The curves obtained from the entire group of forty-eight patients before sympathectomy were practically identical with those in Fig. 2 (see Table III) and are therefore not presented.

A

REACTION OF BLOOD SUGAR TO INTRAVENOUS INSULIN  
(BEFORE SYMPATHECTOMY)



B

age and Q is 1 P all expressed as decimals. If the ratio of the difference between the values in question and the standard error of those values is not greater than 2, the difference can be considered due to chance.

# RESULTS

1 *The fasting blood sugar level in patients with hypertension before and after sympathectomy.* The concentration of reducing substances in the blood of forty-eight fasting patients with hypertension varied from 79 to 118 mg per cent. The mean was 88 mg per cent. In the entire group of thirty-three postoperative patients the average fasting blood sugar was also 88 mg per cent. In the group of twenty-two patients who had test done between stages of sympathectomy the average fasting blood sugar level was 93 mg per cent. There was no significant difference among these values.

TABLE I THE FASTING BLOOD SUGAR LEVEL IN HYPERTENSIVE PATIENTS BEFORE AFTER AND BETWEEN STAGES OF SYMPLECTOMY (MILLIGRAM PER CENT)

RELATION TO SYMPLECTOMY	AGE		
	NO. PAT.	MAST M.M.	MI M.
Before	48	118	7
After	33	102	
Between stages	22	113	7

When the average fasting blood sugar levels of the same twenty-nine patients in whom tests were done both before and after lumbodorsal sympathectomy were compared, again no difference was observed. Similarly the average blood sugar level in sixteen patients who had interim as well as preoperative and postoperative tests was well within normal limits and not significantly different from the values before and after completion of the sympathectomy. The figures are presented in detail in Table I. This lack of difference between the blood sugar levels in subjects before and after sympathectomy is in agreement with the data reported in animal (Cannon, M. Iyer and Blum, Britton, Gellera and Calvert, DuRoi, Schlusberg, Sawyer and Bixby, McDonough, Bousha, Cannon and Dill).

2 *The reaction of the blood sugar to the test in patients with hypertension before sympathectomy.* Forty-eight patients were tested. Of these only twenty-nine eventually had completion of both stages of sympathectomy. Figure 1 represents the insulin tolerance curves for the group of twenty-nine patients in whom determinations were made both before and after sympathectomy. In Figure 2, A, the blood sugar concentrations are presented as changes from the fasting level in milligram per cent. In Figure 2, B, the blood sugar values are expressed as per cent of the fasting blood sugar. Each point in the curve represents a mean of several determinations (Table II) and the

It will be noted that, preoperatively the lowest points in the insulin tolerance curves occurred on an average of 3 ( $\pm 6.4$ ) minutes after the intravenous injection of insulin. The earliest nadir occurred 4 minutes after the injection; the latest, 30 minutes. Hypoglycemia in response to insulin developed more slowly in these patients than had been observed in normal individuals by Fraser

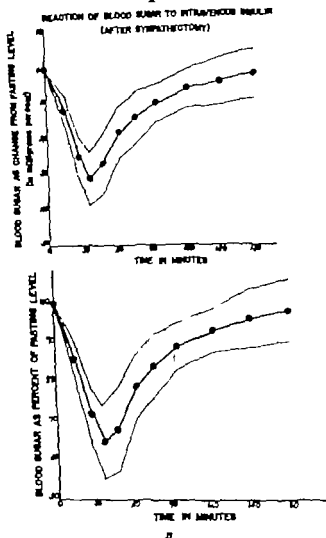


FIG. 1.—The cooperative insulin tolerance curve after lumbar-sympathectomy in the same twenty-nine patients represented in Figs. 2, 4 and 5 in Fig. 1. The shaded areas represent the 4 standard deviations of the determinations from the mean.

Albright, and Smith (20 to 30 minutes) and by Brace and Meduna, and Vaschali (30 minutes). The explanation for this slower development of hypoglycemia after the injection of insulin in hypertensive patients as compared with normal individuals is not apparent. The phenomenon may be characteristic of the disease, or it may be due to the fact that the normal controls in the group reported by Fraser, Albright and Smith were sensitized to insulin by the high

TABLE II THE REACTION OF THE BLOOD SUGAR TO THE INTRA VENOUS INJ. MIX OF INSULIN (0.03 UNITS PER KILOGRAM OF BODY WEIGHT) IN PATIENTS WITH HYPEREMIA (ALL CASES INVOLVED EXTREMES AS PER CHART OF F. WING LAY.)

TIME AFTER INJECTION* (MIN)	BEFORE SYMPATHECTOMY (48 HRS)						BETWEEN STAGES OF SYMPATHECTOMY (23 CASES)						AFTER SYMPATHECTOMY (23 CASES)					
	MAXI MUM	MINI MUM	MEAN	M	N		MAXI MUM	MINI MUM	MEAN	M	N		MAXI MUM	MINI MUM	MEAN	M	N	
	(%)	(%)	(%)				(%)	(%)	(%)				(%)	(%)	(%)			
Before injection	91	56	74	9.8	20	23	44	—	100	—	—	—	—	—	100	—	—	—
15-30	41	8	9	16	20	23	23	94	78	85	17	11	94	61	80	46	10	23
30-35	55	16	20	14.0	21	20	20	94	61	85	29	9	94	65	70	77	16	23
35-40	64	23	43	10.4	16	47	47	91	49	65	8.7	1.9	85	44	66	92	18	49
40-45	77	34	56	9.8	15	30	30	—	—	—	—	—	—	—	—	—	—	—
45-55	84	37	65	15.0	25	23	23	8	34	71	9.0	2.0	—	—	—	—	—	—
55-70	93	83	71	9.8	1.8	41	41	8	64	80	6.2	1.6	92	59	72	81	15	49
70-85	94	94	94	9	1.5	40	40	101	75	86	7.7	1.8	96	63	84	75	18	19
85-106	123	148	94	11.1	3.0	40	40	101	78	90	6.5	1.4	102	79	88	60	11	48
103-140	156	90	94	13.2	1	41	41	104	91	93	7.5	1.6	115	80	93	85	10	23
125-165	120	83	94	7.7	1.3	41	41	104	94	94	7.7	1.6	115	80	93	85	10	23
180-197	128	85	94	9	1.7	34	34	106	92	94	7.8	1.6	110	78	90	81	14	29

\*The times are recorded with a watch to include all the groups since the mean times for the points on the curve are not identical for all the groups. The area under each of the groups can be read from the curve illustrated in the figure.

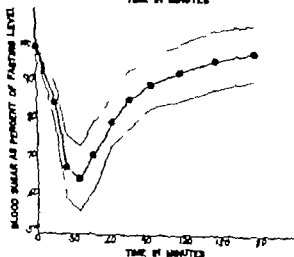
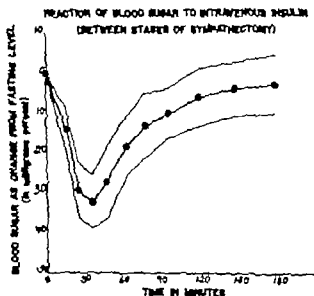
TABLE III THE REACTION OF THE BLOOD SUGAR TO THE INTRA VENOUS INJECTION OF INSULIN (0.03 UNITS PER KILOGRAM OF BODY WEIGHT) IN PATIENTS WITH HYPEREMIA (ALL CASES INVOLVED EXTREMES AS CHART FROM F. WING LAY, IN MILLIGRAMS PER CCM)

TIME AFTER INJECTION* (MIN)	BEFORE STAMP SYMPATHECTOMY (48 HRS)						BETWEEN STAGES OF SYMPATHECTOMY (23 CASES)						AFTER STAMP SYMPATHECTOMY (23 CASES)					
	MAXI MUM	MINI MUM	MEAN	M	N		MAXI MUM	MINI MUM	MEAN	M	N		MAXI MUM	MINI MUM	MEAN	M	N	
	(%)	(%)	(%)				(%)	(%)	(%)				(%)	(%)	(%)			
Before injection	—	—	0	—	—	—	—	—	0	—	—	—	—	—	0	—	—	—
15-30	41	8	9	16	20	23	23	94	78	85	17	11	94	61	80	46	10	23
30-35	55	16	20	14.0	21	20	20	94	61	85	29	9	94	65	70	77	16	23
35-40	64	23	43	10.4	16	47	47	91	49	65	8.7	1.9	85	44	66	92	18	49
40-45	77	34	56	9.8	15	30	30	—	—	—	—	—	—	—	—	—	—	—
45-55	84	37	65	15.0	25	23	23	8	34	71	9.0	2.0	—	—	—	—	—	—
55-70	93	83	71	9.8	1.8	41	41	8	64	80	6.2	1.6	92	59	72	81	15	49
70-85	94	94	94	9	1.5	40	40	101	75	86	7.7	1.8	96	63	84	75	18	19
85-106	123	148	94	11.1	3.0	40	40	101	78	90	6.5	1.4	102	79	88	60	11	48
103-140	156	90	94	13.2	1	41	41	104	91	93	7.5	1.6	115	80	93	85	10	23
125-165	120	83	94	7.7	1.3	41	41	104	94	94	7.7	1.6	115	80	93	85	10	23
180-197	128	85	94	9	1.7	34	34	106	92	94	7.8	1.6	110	78	90	81	14	29

\*The times are recorded with a watch to include all the groups since the mean times for the points on the curve are not identical for all the groups. The area under each of the groups can be read from the curve illustrated in the figure.

3 The reaction of the blood sugar to intravenous insulin between stages of sympathectomy and after bilateral lumbodorsal sympathectomy. Fig. 3 shows the insulin tolerance curves after completion of lumbodorsal sympathectomy in the same twenty nine patients whose preoperative tests are illustrated in Fig. 2

A.



B.

FIG. 3.—The comparative insulin tolerance curves in twenty-four patients in whom bilateral sympathectomy was done in the stages of lumbodorsal sympathectomy. A and B. The shaded areas represent the standard deviation of the blood sugar response from the mean.

Curves for the whole group (thirty-three patients in whom sympathectomy was completed) were practically identical with those and are therefore not presented (Table III). The points were computed as means, just as they had been



4) Third, the lowest point in the curve comes later on the average than it does before operation. When tested statistically the difference between the lowest points in the curves before and after operation is well outside the possibility of its being due to chance.

In Fig. 5 are represented curves of insulin tolerance in twenty-two cases in which the test was done in the interim between stages of lumbodorsal sympathectomy. It will be seen that these curves are practically identical with those from the group tested after completion of sympathectomies. Since in the animal unilateral adrenalectomy does not influence the tolerance to insulin it can be concluded that the difference between the insulin-tolerance curves before and after completion of sympathectomy is not a specific effect of operation (Fig. 6). In fact it probably represents a nonspecific effect of a major surgical procedure on the general bodily economy of the patient, carbohydrate metabolism being one component of such a general effect.

4. *Clinical effects of intravenous insulin (0.03 unit per kilogram of body weight) before and after sympathectomy.* In spite of the fact that such small doses of insulin were used clinical signs and symptoms were detectable in the majority of patients before sympathectomy. Pallor or flushing, sometimes alternating in the same patient was commonly observed. Profuse perspiration was common. Weakness, lassitude and drowsiness (leading to sleep) were observed among the severer reactions. No patient had convulsions. In Table IV is listed the incidence of such insulin reactions before and after sympathectomy. Patients recorded as having slight symptoms developed pallor, weakness, and a feeling of unsteadiness. The symptoms were lassitude or moderate when in addition to those just described, there was profuse sweating. Under severe symptoms are listed the patient who, in addition to drenching perspiration became erythematous and slept when left alone. After lumbodorsal sympathectomy reactions to the doses of insulin used were less common and less severe. This finding was unexpected but is consistent with the greater resistance to insulin that these patients exhibited after sympathectomy (Figs. 2 to 6).

#### DISCUSSION

The failure to demonstrate an increased sensitivity to insulin and a decreased ability to recover from hypoglycemia was unexpected in view of the overwhelming amount of data in the literature indicating an increased sensitivity of sympathectomized animal to insulin. One explanation might be that the dosage of insulin used in the test was too small to be discriminative. Schlosberg, Sawyer and Dixie<sup>12</sup> emphasized for the cat and Houmby, Lewis and Molin<sup>13</sup> for the dog. Their underdeterminating doses produced no symptoms, however, while the patient upon whom these tests were done did have reactions, though not universal. Yet instead of an increase in the proportion of patients who developed symptoms in response to insulin after sympathectomy there was actually a decrease in the incidence of hypoglycemic symptoms. Furthermore the average drop in the concentration of the blood sugar in response to insulin before operation was below the level believed necessary to elicit a central excitation of the autonomic nervous system. In fact de Takáts,



before operation and the standard deviations from the means are indicated by the shaded areas. Three features are of interest. First, there is no significant delay in the recovery from hypoglycemia which was expected if these results were to conform with the reported animal experiments. Second, the drop in the concentration of blood sugar is not as great after operation as it is before (Fig.

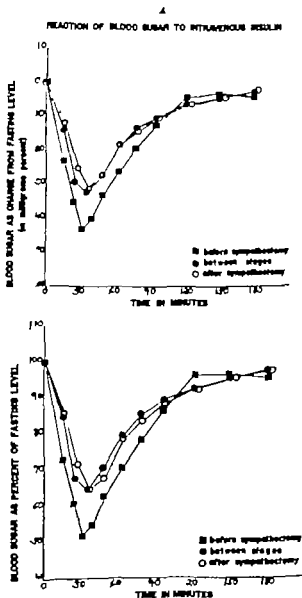


Fig. 4.—The composite insulin tolerance curves before operation, in between stages of operation, and after completion of laparoscopic sympathectomy. A and B as in Fig. 3.

TABLE 1005 U. S. DEPT. OF AGRICULTURE (BY R. L. LORAN AND B. V. VANDER) IN PATIENTS WITH HYPERTENSION AFTER SYMPLECTOMY (29 OPERATIONS)

EXPERIMENT					PER CENT OF PRE-OPERATIVE LEVEL				
BEFORE OPERATION					AFTER LUMBOSACRAL SYMPLECTOMY				
MAX. UREA	MI. UREA	MEAN (G)	M	%	MAX. UREA	MI. UREA	MEAN (G)	M	%
—	—	100	0	0	—	—	100	0	0
91	54	73	8.8	3	91	91	91	4.5	11
4	31	61	13.9	4.8	44	55	2	3	1.6
74	38	50	9	1.9	42	44	65	9.4	0
77	34	35	9.9	0	—	—	—	—	—
84	37	1	1.1	2.1	6	45	44	10.8	1
9	33	71	10	1	9	34	70	0	1.6
97	30	79	9.9	1.9	93	62	84	8.0	1
100	64	8	11.4	6	10	70	6	8.0	1
126	47	97	18.4	7.2	102	60	93	3.4	1.0
119	62	9	7.4	1.4	110	37	96	7.4	1.8
115	49	84	6.6	1	116	76	94	7.9	1

and Browne<sup>11</sup> found that patients excreted 3 to 30 times the normal amounts of cortinlike substances in the urine during the first week after surgical operation. This finding is interpreted as reflecting the elaboration of the "C" or "sugar" hormone from the adrenal cortex. It promotes the deposition of glycogen in the liver and antagonizes the action of insulin. In rats exposed to prolonged stress, Mason<sup>12</sup> observed an initial decreased insulin sensitivity (during the period of alarm) followed by a period of increased sensitivity to insulin during the period of resistance in the general adaptation syndrome. There may be a species difference in this regard, between rat and man, or there may be a different effect from a continually applied stimulus which Mason used. It is interesting in this connection that in 1939 Briouha, Cannon, and Dill observed that in the dog, there was a striking decrease in the glucose tolerance two weeks after symplectomy with return to nearly normal level two days after symplectomy.

The failure to detect an increased sensitivity to insulin in the patient studied is explained, then, by the fact that the tests were done during the period of convalescence when there was probably an increased excretion of cortinlike hormone (Venning, Hoffman and Browne<sup>13</sup>; Tallit, Saltzman, Wooten, and Wolfe<sup>14</sup>) and a decreased excretion of 17-ketosteroids (Forbes, Donaldson, Reifenschein, and Albright<sup>15</sup>). Test done later well after the period of convalescence has been completed, might show a decrease after symplectomy in the ability of such individuals to recover from insulin hypoglycemia such as has been demonstrated in animals. Such a test would be very useful in valuating failure after lumbosacral symplectomy for hypertension. If further study of this problem be made the period of the general adaptation syndrome does demonstrate a sensitization to insulin after symplectomy, it becomes equally important not to postpone the first postoperative insulin tolerance test too long after symplectomy. It should be done before regeneration of the severed or excised sympathetic fibers can have occurred. A test showing a sensitivity to insulin 3 or 4 more after operation would not discriminate between incomplete denervation of the adrenal glands and regeneration of fibers into once-denervated structures.

TABLE IV THE REACTION OF THE BLOOD SUGAR TO THE INTRAVENOUS INJECTION OF TESTES EXTRACTED BLOOD AND

	41	9	23	83	1	11	19	6	1	4.1	10	19
1-20	50	16	5	1.4	3.6	12	22	14	23	4.0	17	17
20-33	62	4	43	10.5	0	24	50	13	31	4	16	23
33-40	65	20	40	6	0	77	—	—	—	—	—	—
40-43	65	13	33	14.0	3.6	15	46	14	77	4.5	17	23
43-55	42	5	—	8.9	1.8	23	35	—	14	7.3	13	23
55-70	41	2	1	9.4	1.4	27	25	2	14	2	17	15
70-85	74	16	1	9.9	2.3	19	70	2	10	5.4	1.1	24
85-100	16	140	4	17	2.6	23	19	13	6	5.3	1.0	24
105-140	14	14	3	6.9	1.1	76	14	4	4	6.7	1.3	27
145-165	11	11	4	8.5	1.4	16	77	14	7.0	1.5	27	27
160-197												

The boxes are recorded in the center to include all the groups under the mean value for the point on the curve or not identical for all the groups. The mean value for each of the groups can be read from the curves illustrated in the figure.

Heyer and Keeton<sup>21</sup> reported a demonstrable difference in the response to insulin before and after sympathectomy when as little as 0.01 unit of insulin per kilogram of body weight was injected intravenously. In less of the kind of patients being investigated, it was certainly desirable to use doses of insulin which would not induce hypoglycemic shock.

A comparison of individual insulin tolerance curves showed no essential difference between those from patients who had the least extensive sympathectomy and those from patients who had the most extensive lumbar sympathectomy. The lack of increased insulin sensitivity in the hypertensive patients is therefore not due to incomplete denervation of the adrenal glands, for these structures were certainly denervated in the most extensive of the lumbar sympathectomies.

The possibility suggests itself that this decreased sensitivity to insulin is a manifestation of metabolic changes induced in patients as a component of the nonspecific effects of a major surgical procedure. That general metabolic changes, related to adrenal cortical function, do occur as a part of the nonspecific response of organisms to stress is well recognized (Selye<sup>22</sup>). Such changes occur following severe injury or major surgical operations. Cope, Nathanson, Rourke, and Wilson<sup>23</sup> observed in severely burned patients a negative nitrogen balance and an initial increase in the urinary excretion of 17-ketosteroid followed by a decrease during the remainder of the convalescence. Fisher, Donaldson, Rosenstein, and Albright<sup>24</sup> observed that in individuals who were previously normal and were operated upon or incurred injury there was a rise in the 17-ketosteroid urinary excretion for one to three days, followed by a fall in the excretion lasting until completion of the convalescence. The 17-ketosteroid excretion is interpreted as reflecting the elaboration of the protein anabolic hormone by the adrenal cortex. There is evidence, on the other hand, that exposure of individuals to stress is attended by an increase in the urinary excretion of 11-oxy corticosteroids (Talbot, Saltzman, Wixson, and Wolf<sup>25</sup>) or of cortinlike substances (Weil and Browne<sup>26</sup>; Venning and Browne<sup>27</sup>). Venning, Hoffman,

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## CONCLUSIONS

1 Shortly after lumbodorsal sympathectomy for hypertension, the response of patients to insulin is increased and the ability to recover from hypoglycemia is not impaired

The significance of these findings is discussed in relation to the metabolic changes in the general adaptation syndrome and to the possible usefulness of the insulin tolerance test in the problems connected with the treatment of hypertension by lumbodorsal sympathectomy

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## CASE REPORT

J. B. aged 41 years a colored porter entered the emergency hospital of the University of Tennessee on July 23, 1934 complaining of (1) swelling of the abdomen and (2) shortness of breath. Eight months prior to admission, the patient noticed some swelling of the ankles. One month later bilateral distention was observed. At this time the patient consulted physician who made a diagnosis of tachycardia and gave the patient at that time a prescription for digitalis abdominal paracentesis as well as for the relief of asthma.



FIG. 1.—Swelling of the abdomen from the front. FIG. 2.—Swelling of the abdomen from the side.

From July 23 to July 27, 1934, the patient was in the hospital. On July 27, 1934, the patient was taken to the operating room for the removal of the swelling of the abdomen. The operation was successful and the patient was discharged on July 28, 1934.

At the time of admission, the patient was in the hospital. The patient was taken to the operating room for the removal of the swelling of the abdomen. The operation was successful and the patient was discharged on July 28, 1934.

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## COMBINED CERVICAL AND THORACIC APPROACH FOR RESECTION OF LARGE ARTERIOVENOUS ANEURYSM

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A WIDE experience in the management of arteriovenous fistula was gained during World War II resulting in the publication of much valuable material on this subject. However these battle casualties were seen and treated relatively early. The purpose of this communication is to describe the pathologic effects and management of a case of twelve years duration.

Arteriovenous fistulas were recognized in 1757 by John Hunter. However the true nature of the pathologic physiology caused by such lesions was not fully appreciated until comparatively recent times.

It was in 1920 that Mont Reid stated that he believed an arteriovenous aneurysm caused serious cardiac disturbances which might be relieved or prevented by curing the arteriovenous fistula. This opinion was based upon experiment performed upon dogs, carried out in the experimental laboratory of Dr. W. S. Halstead. Halstead had previously noticed that cardiac hypertrophy was present in many patients suffering from large arteriovenous fistulas. The accuracy of Reid's concept has since been confirmed many times by both clinical and experimental observations. The studies of Holman, Reed, Callander and Matas are especially significant.

In a discussion of the factors which influence the development of cardiac hypertrophy in cases of arteriovenous fistula, these mentioned the size of the vessels involved, the size of the fistula and the proximity of such fistula to the heart. Harrison, Dock, and Holmes showed that a large arteriovenous fistula favors the development of a increase in the blood volume of the individual.

The first patient, to my knowledge with an arteriovenous fistula involving the subclavian vessels to be cured by operation was operated upon in 1900 by Matas, and was reported upon in 1902. Matas has made significant contributions to the better understanding and management of blood vessel injury in the intervening years. World War II produced more such injuries than had ever before been seen. Numerous post mortem studies were made by members of this society and others who cared for patients on service hospital.

This presentation is based upon a single case treated in civilian practice since our return from the service. It is presented primarily for two reasons: first, because it demonstrates most dramatically the venous changes which are to be expected from a large arteriovenous fistula in which treatment is long delayed, and, second, because it illustrates a type of case which technically is managed most safely by a combined cervical and thoracic approach.

## CASE REPORT

J. M. aged 31 years, colored port entered the teaching hospital of the University of Tennessee on Jan. 13, 1934, complaining of (1) swelling of the abdomen and (2) shortness of breath. Eight months prior to admission, the patient noticed some swelling of the ankles. One month later abdominal distention was observed. At this time the patient consulted physicians who made diagnosis of early renal disease and who gave the patient intravenous injections and performed bilateral paracentesis on occasion for the relief of ascites.



Fig. 1—Pre-operative view of cervical region on dissection. Small scar on left side of neck is result of old stab wound. Small scar on right side of neck is result of old stab wound. Fig. 2—Post-operative view of chest demonstrating incision and drainage.

**History.**—Treatment for syphilis given in 1910 and 1911. In April, 1934, the patient received at least one such box the mid portion of the left clavicle. The upper limb could not be moved. Several weeks later palpating mass appeared over the clavicle and the veins became engorged.

**Examination.**—Examination revealed an enormous dilatation of the vein in the left cervical region. The vein was tortuous and extended from the left side of the neck to the base of the left ear. The dilated vein was extended to the right of the midline of the neck. The vein was palpable at the midpoint of the left clavicle. The vein was 6 to 7 cm. in diameter. The vein was palpable as a pulsating mass with a measured pressure of 61 mm. Hg. A strong thrill was palpable. The vein had continuous machinery-like sounds heard on auscultation. It appeared to obliterate the pulsations of the carotid artery by pressure. The vein was palpable all from below the clavicle to the neck.

The heart was fully enlarged, the point of maximum impulse being at the sixth intercostal space. The blood pressure was 120/80, the pulse 100 and the respiratory rate 20 per minute. The abdomen was distended with fluid. The lower extremities revealed pitting edema below the knees.



## COMBINED CERVICAL AND THORACIC APPROACH FOR RESECTION OF LARGE ARTERIOVENOUS ANEURYSM

HARVEY WILSON, M.D. AND (BY INVITATION) DUANE CARR, M.D.  
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*(From the Department of Surgery of the University of Tennessee)*

A WIDE experience in the management of arteriovenous fistula was gained during World War II resulting in the publication of much valuable material on this subject. However, these battle casualties were seen and treated relatively early. The purpose of this communication is to describe the physiologic effects and management of a case of twelve years' duration.

Arteriovenous fistulas were recognized in 1757 by John Hunter. However, the true nature of the pathologic physiology caused by such lesions was not fully appreciated until comparatively recent times.

It was in 1920 that Mont Reid stated that he believed an arteriovenous aneurysm caused venous cardiac disturbances which might be relieved or prevented by curing the arteriovenous fistula. This opinion was based upon experiments performed upon dogs, carried out in the experimental laboratory of Dr. W. S. Halstead. Halstead had previously noted that cardiac hypertrophy was present in many patients suffering from large arteriovenous fistulas. The accuracy of Reid's concept has since been confirmed many times by both clinical and experimental observations. The studies of Hillman, Reid, Callander, and Matas<sup>1</sup> are especially significant.

In a discussion of the factors which influence the development of cardiac hypertrophy in cases of arteriovenous fistula, Gage<sup>2</sup> mentioned the size of the vessels involved, the size of the fistula, and the proximity of such a fistula to the heart. Harrison, Dock, and Holman<sup>3</sup> showed that a large arteriovenous fistula favors the development of an increase in the blood volume of the individual.

The first patient, to my knowledge, with an arteriovenous fistula involving the subclavian vessel to be cured by operation, was operated upon in 1900 by Matas, and was reported upon in 1902. Matas has made significant contributions to the better understanding and management of blood vessel injuries in the intervening years. World War II produced more such injuries than had ever before been seen, and numerous important studies were made by members of this society and others who cared for patients in our service hospital.

This presentation is based upon a single case treated in civilian practice since our return from the war. It is presented primarily for two reasons: first, because it demonstrates most dramatically the extensive changes which are to be expected from a large arteriovenous fistula, which treatment is long delayed, and, second, because it illustrates a type of case which technically is managed most safely by a combined cervical and thoracic approach.

Read at the meeting of the Society of Urologic Surgeons, New Orleans, La., Jan. 29-31, 1948.

## CASE REPORT

J. R. aged 41 years, colored port, entered the teaching hospital of the University of Tennessee on Jan. 15, 1947, complaining of (1) swelling of the abdomen and (2) shortness of breath. Eight months prior to admission the patient noticed some swelling of the legs. One month later abdominal distention was observed. At this time the patient consulted physicians who made a diagnosis of cardiovascular disease and who gave the patient intravenous potassium chloride and performed abdominal paracentesis on several occasions for the relief of ascites.



Fig. 1—Anterior view of left cervical region on admission. Incision near lower mid portion of left lung field, lower end of wound reveals left lower pulmonary artery.



Fig. 2—Chest roentgenogram of above demonstrates an enlarged right atrium.

**Past History.**—Treated for syphilis in 1940 and 1941. In April, 1934, the patient received a blow to the neck when the mid portion of the left larynx. The superficial wound healed. Several weeks later pulsating mass appeared above the larynx and the carotid was engorged.

**Examination.**—Examination revealed enormous dilatation of the mass in the left cervical region. The mass was retrosternal and extended from the larynx to the base of the left lung. The dilated mass likewise extended to the right of the midline and superior. One inch superior to the mid point of the left larynx a carotid aneurysm in length of the vessel here was palpated. The mass was 16 by 16 cm. in length. A strong thrill palpable there was not out now much as a like murmur heard on auscultation. Impossible to admit that the patient gave complete relief of pressure as seemed to rise part II from beneath the larynx.

The heart markedly enlarged the position of the normal impulse being heaved on the sternum as a medial base (over xiphoid). The blood pressure was 170/110 pulse 104 and the respiratory rate was 20 per minute. The abdomen was distended with fluid. The lower extremities showed pitting edema below the knees.

## COMBINED CERVICAL AND THORACIC APPROACH FOR RESOLUTION OF LARGE ARTERIOVENOUS ANEURYSM

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MEMPHIS, TENN.

(From the Department of Surgery of the University of Tennessee)

A WIDELY experienced in the management of arteriovenous fistula was gained during World War II, resulting in the publication of much valuable material on this subject. However these battle casualties were seen and treated relatively early. The purpose of this communication is to describe the physiologic effects and management of a case of twelve years' duration.

Arteriovenous fistula were recognized in 167 by John Hunter. However the true nature of the pathologic physiology caused by such lesions was not fully appreciated until comparatively recent times.

It was in 1870 that Alout Reid stated that he believed an arteriovenous aneurysm caused various cardiac disturbances which might be relieved or prevented by curing the arteriovenous fistula. This opinion was based upon experiments performed upon dogs, carried out in the experimental laboratory of Dr. W. S. Halstead. Halstead had previously noticed that cardiac hypertrophy was present in many patients suffering from large arteriovenous fistulae. The accuracy of Reid's concept has since been confirmed many times by both clinical and experimental observations. The studies of Holman, Reid, Calland and Matar are especially significant.

In a discussion of the factors which influence the development of cardiac hypertrophy in cases of arteriovenous fistula, (1) he mentioned the size of the vessels involved, the size of the fistula and the proximity of such a fistula to the heart. Harrison, Dock, and Holman showed that a large arteriovenous fistula favors the development of an increase in the blood volume of the individual.

The first patient, to my knowledge with an arteriovenous fistula involving the subclavian vessels to be cured by operation was operated upon in 1906 by Matar, and was reported upon in 1907. Many have made significant contributions to the better understanding and management of blood vessel injuries in the intervening years. World War II produced more such injuries than had ever before been seen, and numerous important studies were made by members of this society and others who cared for patients on service hospitals.

This presentation is based upon a single case treated in civilian practice since our return from the service. It is presented primarily for two reasons: first, because it demonstrates most dramatically all the vascular changes which are to be expected from a large arteriovenous fistula in which treatment is long delayed, and, second because it illustrates a type of case which technique is managed most safely by a combined cervical and thoracic approach.



FIG. 1.—Photograph of specimen removed. Each clamp occludes an artery and vein. The aneurysm is 4 cm. high.

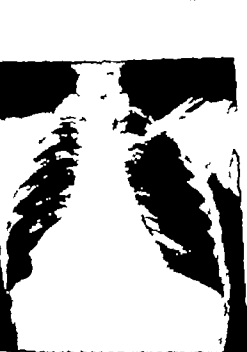
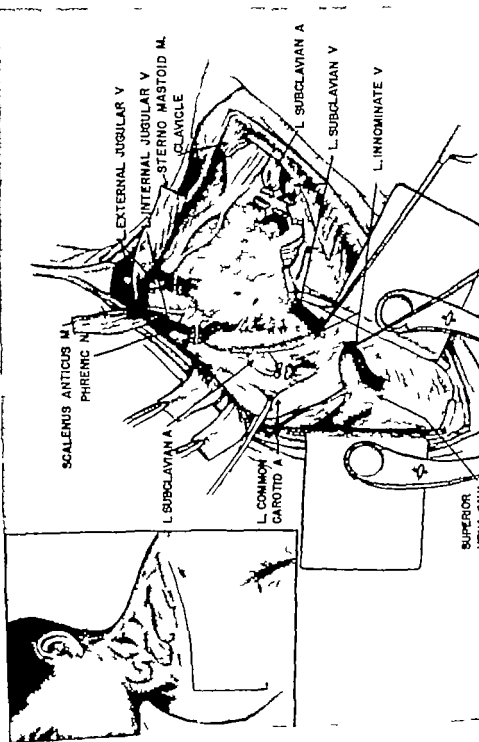


FIG. 2.—Fluorograph taken on 10/10/34. The transverse diameter of the aneurysm is 4 cm. The aneurysm is 4 cm. high.

FIG. 3.—Fluorograph taken on 10/10/34. The transverse diameter of the aneurysm is 4 cm. The aneurysm is 4 cm. high.



## SUMMARY AND CONCLUSIONS

1. The late physiologic effects of arteriovenous aneurysm are discussed and demonstrated in a case which was untreated for twelve years.

The technical considerations involved in the removal of a large arteriovenous aneurysm beneath the clavicle are outlined and the operation which involved resection of the clavicle and opening of the mediastinum through a sternum-splitting incision is described.

3. A follow-up examination of the case described made nine months after operation, revealed that the heart was compensated, the function of the arm normal and the patient was engaged in his former occupation. Regeneration of the left clavicle was found to be taking place.

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*Diagnosis*—Diagnosis as cardiac decompensation, secondary to long standing thoracic aneurysm.

Abdominal paracentesis done and 6,400 cc of ascitic fluid removed. The patient was given digitalis and mercurial diuretics.

The symptoms and signs of cardiac decompensation disappeared rapidly after medical management was instituted. It was the opinion of both the internist and the surgical consultant that the decompensation was secondary to the large arteriovenous aneurysm which had been present for twelve years. It was believed that this represented communication between the left subclavian artery and this was verified at operation.

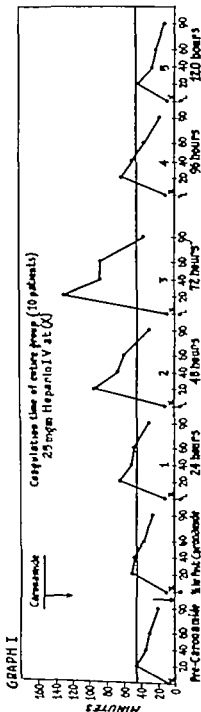
*Operation*—An incision made over the left latissimus beginning near its lateral extremity and extending to the sternal angle junction. The pericostum of the latissimus muscle and the medial three-fourths of the bone removed subperiosteally. A Gelfoam was used to divide the bone laterally and to disarticulate medially from the sternum. The sternocleidomastoid muscle as divided just above the insertion and the rib cage muscles on the ribs on either side were likewise reflected superiorly. It was apparent after this musculocutaneous flap raised that it could not be possible to control the proximal vessels of the aneurysm without opening the thoracic cage. Consequently the sternum divided in the midline just below the third costal cartilage and the sternum was then cut through laterally at this level so that the rib cage could be introduced to open the mediastinum widely. The pleura as not entered. A tape as passed around the innominate vein. The left common carotid as exposed and retracted to the right with an encircling tape so that the left subclavian artery might be better exposed. Compression of the left subclavian artery definitely decreased the tension within the arteriovenous aneurysm. The left subclavian artery as triple ligated and divided. The innominate vein as similarly ligated and divided. The internal and external jugular veins, both of which entered the mass, were ligated and divided. The subclavian artery and vein were next divided just distal to the point at which they cross the first rib. At this point the mass became less tense. However slight thrill as still present. An artery and vein were then found to enter the mass posteriorly. These are believed to be enlarged to anastomose cervical vessels, although their identity not definitely established. The mass as then removed without appreciable loss of blood. At one time during the procedure small tear as made in the wall of the aneurysm and hemorrhage from this area as controlled by digital pressure during the remainder of the dissection.

The operation was performed with atractor and retractor. In the early stages of the operation 1,000 cc of saline solution were given and 1,000 cc of blood were administered slowly during the remainder of the operation. The blood pressure remained stable throughout the procedure. Two Pease drains as placed in the wound and the closure was carried out with interrupted cotton sutures. The incision as brought together with hand sutured silk. At the end of the operation, which required six hours, forty minutes, the patient left the operating room but the radial pulse could not be felt.

*Postoperative Course*—The postoperative course was essentially uneventful. The temperature elevation below 100° F on the second and third postoperative days and then remained thus normal limit. A feeble but palpable pulse appeared in the left wrist the day following operation. The left arm and hand were warm and sensation as normal maximally.

An x-ray examination made four days postoperative revealed decrease in heart size and further decrease as noted on subsequent examination. However the heart remained significantly enlarged. The patient did not complain of pain in the region of the resected latissimus or divided sternum; however there was some weakness of the left arm for several weeks. After few months spent in ambulatory capacity at home, the patient returned to his former work part in an office.

The patient has continued his regular employment and his general condition was found to be satisfactory on examination six months following resection of the sternocleidomastoid aneurysm. A roentgenogram made at this time showed less regression of the left chest wall to its original place. The heart was still enlarged, however. The transverse diameter was approximately one centimeter less than that shown in the earlier films.



Graphs I to IV cou Levy Ohio State University Department of Radiography



# PRACTICAL APPLICATION OF THE HEPARIN-CARONAMIDE REACTION TO THE POTENTIATION OF HEPARIN IN GELATIN MENSTRUUM

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THE effect of the chemical compound, caronamide on the renal excretion of penicillin has been well annotated in the recent medical literature. Caronamide (4-carboxyphenylmethanesulfonanilide) when given orally or intravenously with penicillin, effectively reduces the renal excretion of penicillin and results in a two- to tenfold increase in penicillin blood levels. Since the work of Howell and McDonald,<sup>1</sup> Wilander<sup>2</sup> and Copley and Schoedonk<sup>3</sup> has demonstrated that 10 to 40 per cent of an intravenous injection of heparin is eliminated in the urine within one hour we felt that it would be of interest to determine whether the same relationship exists between heparin and caronamide. We have previously reported our experience with ten patients, and Graph I is an average of the response of these patients.

A survey of Graph I will indicate the reaction that occurs in patients who are given a single 4 Gm dose of caronamide orally followed in one half hour by an intravenous injection of 25 mg of heparin. It should be noted that on the day the drugs are given together there is no appreciable rise in the coagulation response of the patient to the same dose of heparin. The 25 mg of heparin alone injected on successive days, with no further caronamide being given during the course of the experiment. There is a gradual increasing potentiation, reaching a peak on the third day and falling off more rapidly to a normal response on the fifth day.

The main disadvantages of heparin therapy have been a necessity for its frequent administration and its high cost. The demonstration by Loewe<sup>4</sup> of the advantages of heparin in Pitkin's menstruum has largely obviated the former. Heparin/gelatin in our experience has had an equivalent effect on the coagulation time. However at the present time heparin therapy is extremely costly and for this reason, if for no other, its usage is limited.

1948  
Heparin  
Sodium ethyl succinate  
Chondroitin sulfate  
Gelatin  
Dextrose

100 mg  
1/2 cc  
1/2 cc

Kidney-Diet HCl  
penicillin HCl  
sodium acetate acid  
Double distilled  
water

1 ml  
10 ml  
1

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coagulation time at a higher level than by the control injection. A third injection of heparin/gelatin menstruum given 48 hours following the single dose of caronamide resulted in an increased height of response when compared to the peak of the control injection but also very little prolongation.

At the right of the graph is the same patient's response when a different method of administration of caronamide was followed. Starting with the first injection of heparin/gelatin in this experiment, caronamide was given orally.

5 gm every three hours for 48 hours. It will be noted that the response is markedly enhanced with a maximum of 120 minutes compared to 75 minutes for the control injection. However there was no prolongation of the effect. At the end of this 48 hour period, a second injection of heparin/gelatin did not produce as marked an effect as the control, but did show an appreciable prolongation of the effect. The third and fourth doses demonstrated the increasing sensitivity that is occurring up to the sixth day following the last dose of caronamide and is manifested by a peak coagulation time of 190 minutes with the same amount of heparin that in the control period gave only a maximum of 75 minutes.

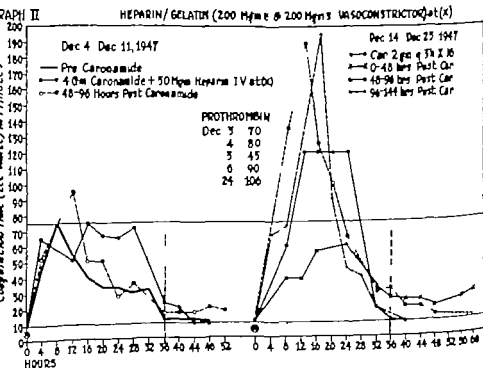
The response to 400 mg of heparin/gelatin in seven case studies verifies the impression gained by the study of the caronamide-heparin reaction previously demonstrated by the use of intravenous heparin, namely that the height of the response was markedly increased but the effect was not beneficially prolonged. With this in mind we studied next the effect of one half the amount of heparin to determine whether this increased sensitivity following caronamide would result in raising the effect of the smaller dosage into the therapeutic zone.

Graph III is a representative response of one of four patients given oral caronamide in 5 gm doses every three hours for 4 hours during the first injection of 200 mg of heparin/gelatin. Each subsequent injection was given at 48 hour intervals. It will be noted that the control curve in this patient was always below the suggested therapeutic range of 15 to 30 minutes. However during the first 4 hours of combined therapy the peak response rose to 34 minutes, but gain was not prolonged over the control. The second injection which covered the period of 24 to 72 hours after the caronamide was stopped, shows a marked increase in effect with a peak of 75 minutes coagulation time at the 1 hour sample and also a secondary rise from 32 to 44 hours following the injection. Hence this injection maintained a therapeutic level for almost 40 hours. The third injection (72 to 120 hours postcaronamide) showed an even greater sensitivity with some prolongation over the control response. During the injection covering the period of 120 to 168 hours after caronamide the response returned to normal.

As demonstrated in Graph I when caronamide was given orally in 4 gm doses followed by 1 gm of intravenous heparin, the response on that day was not significantly higher than the response to the heparin alone in the control phase. In an effort to find some other method of sensitizing patients with caronamide 4 were injected with 3 gm of caronamide and 40 mg heparin

## METHODS AND RESULTS

Since our original experiment indicated that there was no marked prolongation of the effect of a single injection of heparin, but rather a consistent enhancement of the height of response, the practical approach to reducing the cost seemed to be in lowering the amount and not in decreasing the interval between injections. We therefore studied fifteen postoperative patients, who were being treated prophylactically with heparin/gelatin men-strium. Seven patients received 400 mg and eight were given 200 mg every other day. The response of these fifteen patients to heparin and caronamide form the basis for this report. These results indicate that it may be possible to obtain the proper combination of the drugs that will reduce the cost of heparin therapy by 50 per cent.



Graph II shows the reaction of a representative patient to two combinations of heparin and caronamide. On the left will be noted the pre-caronamide response to 400 mg of heparin/gelatin men-strium. At the end of the first 48 hour period the patient was sensitized by the administration of 4 Gm of caronamide orally followed in one-half hour by 50 mg of heparin, given intravenously. Immediately following this sensitization a injection of 400 mg of heparin/gelatin was given. The response indicates only slight prolongation of the total length of effect. There is, however maintenance of the

both given simultaneously by the intravenous route. When the coagulation time had returned to normal following this method of sensitization, each of these patients was given the first postcaronamide injection of 900 mg of heparin/gelatin.

Graph IV is of a representative case of a group of four so treated. It will be noted that during the first injection after caronamide the peak of the response was no higher than the control but it was markedly prolonged, staying in the therapeutic range for almost 48 hours compared to 24 hours in the same patient during the control phase. The second postcaronamide injection showed a similar reaction to the first. However the third and fourth injections, the latter covering the period 150 to 198 hours after the single dose of caronamide showed marked increase of coagulation time response to a peak of 6 minutes, compared to the control peak of 39 minutes. A clearly visible there is a general elevation of the terminal part of the curve following each of these small injections of heparin/gelatin.

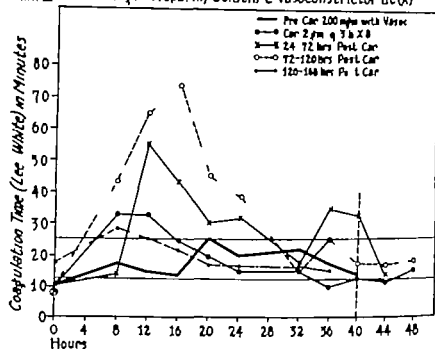
A study of Graph III and IV demonstrates that administration of oral caronamide results in increased sensitivity in the first, second, and third 48 hour periods that intravenous caronamide produces potentiation of the second, third, and fourth injections. These responses suggest that combination of both methods of sensitization would be antagonistic in reducing the amount of heparin necessary for a therapeutic course of eight day duration.

#### DISCUSSION

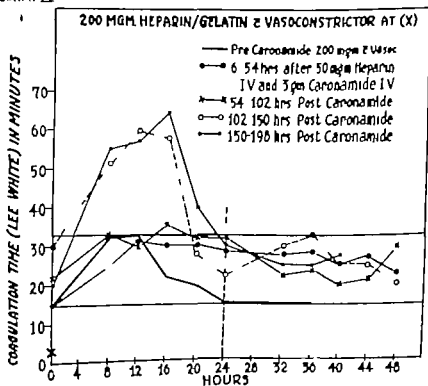
It seems clear at the present time that the practical method of reducing the cost of heparin therapy is the use of caronamide apparently does not lie in the direction of an increased duration of the effect of the usual dosage of heparin/gelatin. Marked elevation of the coagulation time above the suggested therapeutic level of 30 to 40 minutes is probably unnecessary (see Graph II). In light was given on half the usual dose that is, 900 mg heparin/gelatin with vasoconstrictor therapeutic levels were obtained in all cases for a significant period. It was an identical amount in the same patients, during the pre-caronamide phase, did not give a therapeutic response for a appreciable length of time. It is reasonable to suggest that the difference might be expected on the basis of the results demonstrated in increased sensitivity to heparin of patients previously sensitized by caronamide and heparin injections. The potentiation of heparin has occurred in 100 per cent of cases studied. Presumably the heparin in gelatin menstruum is liberated at a relatively constant rate. It is probable therefore that these minimal ultrafiltrate quantities of heparin liberated during the period 24 to 48 hours after injection, will produce a considerable increase in duration of effect.

There has been no toxic reaction manifested in any of the instances in which caronamide and heparin have been administered together. The persons reporting the effect of caronamide alone with penicillin have been so numerous that no deleterious response to caronamide should have appeared. The most interesting side effect which we have noted is the frequent

GRAPH III 200 Mgm Heparin/Gelatin & Vasoconstrictor at (X)



GRAPH IV



# EXPERIENCES IN THE SURGICAL TREATMENT OF PULMONARY STENOSIS

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## INTRODUCTION

MUCH more has appeared in the new papers and magazines about the surgical treatment of patients with pulmonary stenosis than has appeared in the surgical literature. For this reason we have deemed it worth while to record our experiences and impressions acquired during the past one and one half years in the treatment of a relatively small series of forty-three patients in whom a diagnosis of pulmonary stenosis was made. Thirtynine of these patients were treated at the University of Minnesota Hospitals in Minneapolis, Minn., one was treated at the Buffalo General Hospital in Buffalo, N. Y., and three at the Children's Hospital in Buffalo.

Tausig and Blalock opened an entirely new and fascinating chapter of surgery in 1941. To these pioneers all honor should be given. Our own interest in the surgical treatment of pulmonary stenosis derives directly from their paper published in 1944. In the first fifteen cases of the present series, the technique of vascular anastomosis employed by Blalock at the Johns Hopkins Hospital was followed as closely as possible.<sup>1</sup> In the remaining cases, certain minor changes in technique were made as seemed desirable. By fortunate circumstances a Millikan oximeter was available for use in the treatment of many of our cases. A report of this experience has already been made by Gullickson and Hammon.<sup>2</sup>

## REPORT OF CASES

In Table I some of the pertinent data on each patient has been tabulated for the sake of comparison. Forty-five operations were performed on forty-three patients. Twenty-one of these patients were males and twenty-two were females. The oldest patient was 4 years and the youngest was 19 months. Only three children under 3 years of age were accepted for operation. The average age was 4 years.

A preoperative diagnosis of tetralogy of Fallot was made in each case only after careful study by a group of doctors which included a cardiologist, a pediatrician, a roentgenologist and a surgeon. No unusual diagnostic method were used. Those lesions identified with the tetralogy of Fallot are shown in Fig. 3. Catheterization and cardiography were not employed. In any case in which the diagnosis seemed questionable the pressure in the pulmonary artery was measured at the time of operation by means of a water manometer filled with 40 per cent sodium nitrate solution. In no case however was a

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occurrence of an apparently rising prothrombin level during the course of the therapy (see Graph II). No satisfactory explanation for this is yet at hand.

The data submitted suggest that the combination of both demonstrated method of sensitization may result in such enhancement of heparin therapy that a therapeutic response may be obtained with one-half the usual dose of heparin/gelatin. A further test of this thesis is in progress at the present time and it is feasible that the cost of heparin therapy may be reduced by even more than 50 per cent.

#### SUMMARY

1. The heparin-carotamide enhancement of the therapeutic effectiveness of heparin/gelatin menstrogram has been demonstrated in fifteen case studies.

The practical application of this reaction may be expected to reduce the cost of heparin therapy approximately 50 per cent.

The authors wish to express their appreciation to Mrs. Letti S. Robinson for her technical assistance.

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15. Winkler, O. H. *Abstracts of the American Medical Association*, 1947.







No.	Sex	Age	Side	Date	Ref. No.	Left lung artery		Notes	Result	Remarks
						Artery	Vein			
1	F	23	Left	1903	1	Artery	Vein	Artery	Good	Artery
2	F	24	Left	1903	2	Artery	Vein	Artery	Good	Artery
3	F	25	Left	1903	3	Artery	Vein	Artery	Good	Artery
4	F	26	Left	1903	4	Artery	Vein	Artery	Good	Artery
5	F	27	Left	1903	5	Artery	Vein	Artery	Good	Artery
6	F	28	Left	1903	6	Artery	Vein	Artery	Good	Artery
7	F	29	Left	1903	7	Artery	Vein	Artery	Good	Artery
8	F	30	Left	1903	8	Artery	Vein	Artery	Good	Artery
9	F	31	Left	1903	9	Artery	Vein	Artery	Good	Artery
10	F	32	Left	1903	10	Artery	Vein	Artery	Good	Artery
11	F	33	Left	1903	11	Artery	Vein	Artery	Good	Artery
12	F	34	Left	1903	12	Artery	Vein	Artery	Good	Artery
13	F	35	Left	1903	13	Artery	Vein	Artery	Good	Artery
14	F	36	Left	1903	14	Artery	Vein	Artery	Good	Artery
15	F	37	Left	1903	15	Artery	Vein	Artery	Good	Artery
16	F	38	Left	1903	16	Artery	Vein	Artery	Good	Artery
17	F	39	Left	1903	17	Artery	Vein	Artery	Good	Artery
18	F	40	Left	1903	18	Artery	Vein	Artery	Good	Artery
19	F	41	Left	1903	19	Artery	Vein	Artery	Good	Artery
20	F	42	Left	1903	20	Artery	Vein	Artery	Good	Artery
21	F	43	Left	1903	21	Artery	Vein	Artery	Good	Artery
22	F	44	Left	1903	22	Artery	Vein	Artery	Good	Artery
23	F	45	Left	1903	23	Artery	Vein	Artery	Good	Artery
24	F	46	Left	1903	24	Artery	Vein	Artery	Good	Artery
25	F	47	Left	1903	25	Artery	Vein	Artery	Good	Artery
26	F	48	Left	1903	26	Artery	Vein	Artery	Good	Artery
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28	F	50	Left	1903	28	Artery	Vein	Artery	Good	Artery
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61	F	83	Left	1903	61	Artery	Vein	Artery	Good	Artery
62	F	84	Left	1903	62	Artery	Vein	Artery	Good	Artery
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78	F	100	Left	1903	78	Artery	Vein	Artery	Good	Artery

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ATTN	SEX	AGE (YR)	POS. OF TUMOR	PRES. IN FILM OF ART. (CAL. MAG.)	% OBTAIN.		ONLY TROV	COMPLICATIONS	CLINICAL RESULTS
					PER	ARTERIAL BLOOD			
13 J M	M	2	Right	25	17.5	31	Arteriosclerosis left subclavian art. ; left pulmonary art.	Probable thrombosis of anastomosis	Y improved
14 M D	F	9	Left	49	54.0	73.4	Arteriosclerosis left subclavian art. to left pulmonary	Plural effusion	Good
16 R L	F	4	Left	53	14	6.9	Arteriosclerosis left subclavian art. ; left pulmonary art.		Good
18 M V	P	17	Right	4	50.9		Thrombosis left chest subclavian on basis for arteriosclerosis	Plural effusion	Good
17 K H	P	6	Left	9	54	60	Arteriosclerosis right subclavian art. ; right pulmonary art.	Plural effusion	Good
19 L R	M	1	Left	11	3.3	43	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
19 V Z	F	6	Right		64.9	71	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
20 D B	P	4	Left	4	73.3	53.8	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion; enlargement for 4 days after operation	Good
21 K M	M		Left		67		Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
22 K P	M	5	Left		31.6	1.0	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
23 P L B	F	11	Left		3	67.9	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
24 A	P	29	Left	4	71.3	8.5	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
25 J P	M	6	Left	2	7.9	77.0	Arteriosclerosis left subclavian art. ; left pulmonary art.	Plural effusion	Good
26 B K	P	9	Left		3	68	Arteriosclerosis left subclavian art. ; left pulmonary art.	Ch. lesions, probable thrombosis of anastomosis	Y improved
27 I M	M	4	Right	24	69.4	60.5	Arteriosclerosis right subclavian art. ; upper branch of right pulmonary art. ; left end	Plural effusion, thrombosis of anastomosis	Good
								Arteriosclerosis, probable thrombosis of anastomosis	

been striking. The most notable changes have been a decrease in the cyanosis and polycythemia and an increase in the oxygen saturation of the arterial blood associated with increased physical endurance.

The percentage of saturation of the arterial blood with oxygen was measured before and after operation in thirty-two patients. The postoperative measurements were in most cases taken at least ten days after operation. In three of these cases unsatisfactory clinical result was thought to have been obtained, and there was practically no change in the oxygen saturation of the arterial blood. In the twenty-nine patients in whom the clinical improvement was considered to have been satisfactory the percentage of oxygen saturation of the arterial blood was increased after operation except in three instances (M. M. No. 702, J. P. No. 704, S. F. No. 623, 39). Two of these patients actually showed a postoperative value lower than the preoperative value yet clinically the condition of each seemed to have been definitely improved by the operation.

This occasional lack of correlation between the change in arterial oxygen saturation and the clinical improvement of the patient subsequent to operation has been puzzling. In such cases one is invariably tempted to discount the accuracy of the blood gas determination or to feel that basal conditions did not obtain at the time the blood samples were taken, despite an attempt at establishing a basal state by means of heavy hard-labor sedation. However the possibility remains that another factor such as the size of the interventricular septal defect, the position and inclination of the septal deflection, or another cardiac abnormality may be influencing the result.

The average increase in the oxygen saturation of the arterial blood in those patients clinically improved after the operation was 15 per cent. The greatest increases noted were 35 per cent and 43.6 per cent. In both of these cases the aortic arch artery was explored for the anastomosis.

TABLE III. RESULTS OF OPERATION

Total patients		32
Total operations performed		37
1. Clinical results as follows:		
a. Complete	40	
b. Partially improved	31	
c. Not improved	5	
d. Died	4	
2. Thoracotomy with exploration of aorta:		5
a. Results as follows:		
i. Improved	2	
ii. Not improved	3	
iii. Died	1	

**Postoperative Complications.**—The most common postoperative complication encountered was pleural effusion. A certain amount of effusion was present in almost every case. In ten out of four patients the effusion was of sufficient amount to be of clinical significance and in eight of these cases in eight patients had one or more aspirations of pleural fluid because of dyspnea. No patient developed pyothorax but all were given 40,000 to 100,000 units of penicillin intramuscularly, very three hours for one week after operation, prophylaxis against infection.

pressure measured which was interpreted as contraindicating the construction of a vascular shunt. The pulmonary arterial pressure was determined in twenty-eight cases. The lowest pressure measured was 6 cm. of water and the highest was 35 cm. of water. The majority of pressure recordings varied between 15 and 25 cm. of water but one of the best clinical results obtained was in a 6-year-old Canadian girl who had a pressure of 35 cm. of water in the left pulmonary artery.

The aorta was found to arch to the right in nine patients and to the left in thirty-four patients.

*Operative Procedure Employed*—In four cases the mediastinum was explored but no systemic artery found on the exposed side which was suitable for anastomosis with the pulmonary artery. Two of these patients were operated upon a second time after an interval of several months and a successful anastomosis was completed, through the opposite thoracic cavity.

The common carotid artery was not employed in any case for the construction of a vascular shunt. The innominate artery was employed three times in the construction of an end-to-side anastomosis with the left or right pulmonary artery.

The subclavian artery was anastomosed to the right or left pulmonary artery thirty-seven times. In thirty-five instances an end-to-side type of anastomosis was constituted and in two instances the subclavian artery was joined to the proximal end of the severed uppermost branch of one of the pulmonary arteries.

*Result of Operation*—Six of the forty-three patients died. Five of these patients died in the hospital and on six weeks after leaving the hospital. The hospital mortality was 14 per cent and the total mortality was 14 per cent.

Of the thirty-seven patients who survived operation, thirty-six had a successful shunt completed. The result in fifteen of these cases were unsatisfactory. There was no improvement noted in their appearance, their physical capabilities were unchanged, and the per cent of oxygen saturation of the arterial blood as well as the polycythemia remained relatively unchanged. The lack of improvement in these patients has been ascribed to the formation of a thrombus at the site of the anastomosis in three instances and at the site of the clamp applied to the subclavian artery in the fourth case.

The remaining twenty patients (54 per cent of the total number) have been improved to a varying degree. In most instances the degree of improvement has

TABLE II

	WELL	DEATH
	3	3
	3	1
	21	1
		0
	44	6

been striking. The most notable changes have been a decrease in the cyanosis and polycythemia and an increase in the oxygen saturation of the arterial blood associated with increased physical endurance.

The percentage of saturation of the arterial blood with oxygen was measured before and after operation in thirty-two patients. The postoperative measurements were in most cases taken at least ten days after operation. In three of these cases unsatisfactory clinical results were thought to have been obtained, and there was practically no change in the oxygen saturation of the arterial blood. In the twenty-nine patients in whom the clinical improvement was considered to have been satisfactory the percentage of oxygen saturation of the arterial blood was increased after operation except in three instances (M M No 77025 J P No 77048 E K No 82359). Two of these patients actually showed a postoperative value lower than the preoperative value yet clinically the condition of each seemed to have been definitely improved by the operation.

This occasional lack of correlation between the change in arterial oxygen saturation and the clinical improvement of the patient subsequent to operation has been puzzling. In such cases one is invariably tempted to discount the accuracy of the blood gas determination or to feel that basal conditions did not obtain at the time the blood samples were taken, despite an attempt at establishing a basal state by means of heavy barbiturate sedation. However the possibility remains that another factor such as the size of the interventricular septal defect, the position and inclination of the septal deflection, or another cardiac abnormality may be influencing the result.

The average increase in the oxygen saturation of the arterial blood in those patients clinically improved by the operation was 15 per cent. The greatest increases not 1 were 34 per cent and 43.6 per cent. In both of these cases the aortic anastomosis was employed for the anastomosis.

TABLE III    RESULTS    MORTALITY

Total patients	41	
Total operations performed	47	
A. A. in anastomosis completed		40
Patients improved	31	
Patients not improved	8	
Died	4	
B. Thoracotomy with exploration of aortic aneurysm only		3
Died		
Patients improved		100%
Patients not improved		14%
Patients died		14%

Postoperative Complications.—The most common postoperative complication encountered was pleural effusion. A certain amount of effusion was present in almost every case. In twenty-four patients the effusion was of sufficient amount to be of clinical significance and a source of some concern. Eight patients had one or more aspirations of pleural fluid because of dyspnea. A patient required thoracentesis but all were given 20,000 to 40,000 units of penicillin intramuscularly over three hours to one week after operation as prophylaxis against infection.

Three patients developed a chylothorax in the postoperative period. These patients all responded to repeated thoracentesis with the injury of the lymphatic duct healing spontaneously. Chyle ceased to accumulate in one patient (M. J. C. No. 71663) after ten days, in a second patient (B. H. No. 779013) after twenty-four days, and in the third patient (J. A. T. No. 781169) after fourteen days.

Five patients exhibited varying degrees of a Horner's syndrome after operation. This was invariably on the same side as that of the thoracotomy. In all such patients this was a transient paresis or paralysis and gradually disappeared after a few days or shortly after discharge from the hospital.

Diffuse brain damage due to inadequate oxygenation during operation occurred in three patients. In two instances consciousness was never regained after operation and death occurred on the third postoperative day. The third patient was lethargic for four days after operation, but recovered completely with a very satisfactory clinical result.

Many of the patients in this series have exhibited a slight increase in the size of the heart after operation. This was noted in the first patient operated upon and together with other signs which were considered to be indicative of a mild cardiac decompensation, occasioned the administration of digitalis for a few days. With increased experience less attention has been paid to minor degrees of cardiac enlargement. No instances of definite cardiac decompensation have been observed.

Gangrene of the right hand after division of the right subclavian artery occurred in one patient. This patient was an 18-month-old girl in a desperate condition. The preoperative oxygen saturation of the arterial blood was 15.4 per cent. She had been intensely cyanotic ever since birth and had experienced several convulsive attacks. There was a partial atrophy or hypoplasia of the entire right side of the body. No pulse could be detected at the right wrist. The aortic arch was to the left. The use of the right subclavian artery instead of the left in the construction of the arterial shunt was probably an error of judgment. No other examples of circulatory insufficiency have been observed in the thirty-seven patients in whom a subclavian artery was divided. In patient B. O. (No. 772223) both subclavian arteries were divided without compromising the viability or function of either arm.

The remaining postoperative complication which was observed occurred as isolated instances, and requires no special comment.

*Cause of Death*—Five of the six deaths occurred in the first eleven patients who were operated upon. Some such proportion as this might well be expected by any surgeon who agrees to embark on such a new and treacherous field as that provided by the patient with pulmonary stenosis. Each of these deaths taught important lessons, but the price of experience in this field is high.

Two deaths can be directly attributed to increased relative anoxemia of the brain during the period of anesthesia and operation which was prolonged in both cases. Cyclopropane and oxygen administration through an intratracheal tube was the anesthetic technique employed. Neither of these patients regained con-

sciousness after completion of the operation and 14th died approximately three days after operation. One patient, a 7-year-old boy with a preoperative arterial oxygen saturation of 48.9 per cent had the bronchial artery anastomosed to the right pulmonary artery. Technically this appeared to be a very satisfactory operation and most of the preoperative cyanosis disappeared within a few hours after operation. Consciousness was not regained, however and after twelve hours respiratory paralysis developed. The patient was placed in a Drinker respirator where he remained until death. Marked liquefaction of the entire brain was found at post-mortem. The other patient was an 18-month-old girl with an arterial oxygen saturation of 13.4 per cent. She had had several convulsions, and there was a hypoplasia of the right half of the body. The right radial pulse was not perceptible. At operation the right subclavian artery was anastomosed to the right pulmonary artery. The use of the right subclavian artery in this particular patient was unwise inasmuch as it was known prior to operation that the right side of the body was underdeveloped. Consciousness was never regained following operation and at death there was gangrene of the right hand.

The patient died of cardiac standstill during operation. One of these a girl aged 6 years, with an arterial oxygen saturation of 4.5 per cent, experienced two episodes of losing and regaining of the heartbeat during the dissection of the right pulmonary artery. The injection of 1 per cent Novocain into the vagus nerve and around the hilum of the lung as well as the intravenous administration of atropine sulfate failed to prevent a third and fatal episode of the same kind which occurred during the anastomosis of the right subclavian artery to the right pulmonary artery. The other patient was a boy 18 months old whose heart suddenly ceased to beat shortly after the left side of the chest was opened and immediately after the dissection of the pulmonary artery was begun.

The remaining hospital death occurred in an 8-year-old boy four days after the right side of the chest was explored and the subclavian artery found to be too short for anastomosis. It was planned to explore the left side later but a massive pleural effusion developed in the right side of the chest. When this was aspirated on the fourth postoperative day the patient suddenly died after 30 cc of fluid had been withdrawn.

The sixth death occurred in a 10-year-old girl in whom the left subclavian artery was anastomosed to the left pulmonary artery. The immediate response to operation was excellent and she left the hospital on the sixteenth postoperative day much improved in color and in tolerance of physical exercise. About six weeks later while sitting on the toilet, she suddenly became nauseated, coughed up a large quantity of blood, and died within a few minutes. Post-mortem examination revealed a false aneurysm between the left pulmonary artery and the left main bronchus. In the aneurysmal sac a small cotton pledget was found which had been placed beneath the pulmonary artery during the operation to control some bleeding from a small adhesion vessel.

#### DISCUSSION

The unusual importance of experience in the management of patient with pulmonary aneurysm became evident to us after the first few patients were oper-



ated upon. As soon as possible therefore a team, consisting of a cardiologist, a pediatrician, a roentgenologist, an anesthetist, and two surgeons, was organized to handle these patients. Some such team arrangement, in our opinion is essential if the best results are to be obtained and the mortality kept to a minimum. This conclusion seems to be justified by the fact that no patient has been subjected to operation unnecessarily because of a wrong diagnosis. Furthermore only one patient in the last thirty-two patients of the series has died during operation or afterward. This is in marked contrast to the five patients who died in the first eleven cases.

*Approach and Choice of Vessel*—Blalock has recommended that the anastomosis between the systemic artery and the pulmonary artery be performed on the side opposite to that of the descending aorta. In our first cases this practice was followed closely. The advantage of the exposure thus obtained is that it gives the operator the choice of using either the innominate or the subclavian artery for the anastomosis. The choice of size of vessel is thereby afforded. Furthermore, in those cases in which the subclavian artery is employed, the kinking produced at its origin from the innominate artery is usually less than that produced on the opposite side of the chest at the origin of the subclavian artery from the aorta.

TABLE IV. CAUSES OF DEATH IN SIX PATIENTS

CAUSE	COUNT
Cardiac standstill during operation	1
Result of partial asphyxia during operation	2
Pleural shock during thoracotomy	1
Hemorrhage from bronchobronchial fistula	1

On the other hand, certain disadvantages pertain to the choice of approach which Blalock's recommendations demand. Since only about one out of five patients with pulmonary stenosis have aortas with right lobes, the operator usually finds himself working in the right side of the chest. The arterial anastomosis which must be performed in the right side of the chest is more difficult to execute, more time consuming and, in our opinion, more dangerous than the operation performed in the left side of the chest. The right pulmonary artery lies closely attached to the undersurface of the terminal portion of the superior vena cava and it is difficult to gain a adequate exposure of a sufficient length of the pulmonary artery to perform an anastomosis; the superior vena cava must be so lifted and displaced that the return flow of blood to the heart is often unduly impeded. Furthermore the considerable amount of traction which must at times be exerted on the right pulmonary artery in its dissection and positioning for the anastomosis may interfere with cardiac function. Strong traction on the right pulmonary artery of patient A. G. (N. 64845) produced three episodes of slowing of the heart rate and weakening of the heartbeat with simultaneous cardiac dilatation. Death occurred during the third episode at a time when the traction could not be released.

In addition to the foregoing Blalock's experience has indicated that the mortality in cases in which the innominate artery was employed was about 30 per cent as compared to about 10 per cent in those cases in which the subclavian artery was employed.

For those reasons, and because it was felt that most cases did not require the large shunt provided by an anastomosis of the innominate artery to the pulmonary artery, we arbitrarily decided that all cases in which the preoperative arterial oxygen saturation was over 50 per cent would be approached through the left side of the chest and the subclavian artery used no matter whether the aortic arch was to the right or to the left. In accordance with this idea thirty of the last thirty-one patients have been operated upon through the left side of the chest. So far nothing has occurred to indicate that this is not a good rule. There have been instances in which the available subclavian artery was extremely short. In three cases the artery was too short for any anastomosis and an operation on the other side of the chest was therefore necessary. In a few other cases the artery was so short that extreme kinking at the origin of the subclavian artery from the aorta was present when the anastomosis was completed. This kinking was minimized as much as possible by meticulous dissection of the subclavian artery from all its surrounding tissues and by the arch of the aorta and by a usually freeing the posterior superior and lateral aspect of the arch of the aorta from fascial attachments. This kinking has never interfered with the establishment of an effective shunt nor has it been recognized as the cause of thrombosis.

Experience is still scant at the present time to say with certainty just to what per cent of patients require the flow of blood which the innominate artery can pour into the pulmonary circuit and which patient will receive sufficient improvement from the use of the subclavian artery. It seems only logical to assume however that those patients with extremely low arterial oxygen saturations should be those in whom the surgeon is justified in enlarging the larger arteries with a higher mortality. Further evidence which suggests that the use of the innominate artery may perhaps only rarely be justified is the fact that in this series the two patients showing the greatest increase in the arterial oxygen saturation in less than the venous and two were patients in whom the subclavian artery rather than the innominate was used. The possibility of perforating the pericardium complicating the operation should not be overlooked if the improvement experienced after the first operation is not considered sufficient. The present series contains no example of this but in Scott's (1922) both subclavians were ligated and he died although only one was used for an anastomosis. The nutrition and function of the heart has been unimpaired.

(b) A small experiment is necessary to learn that there is a marked variation in the relationship between the structures in the superior mediastinum and the intercostal space of the anterior chest wall. In most instances a thoracotomy through the third intercostal space anteriorly with division of the third costal cartilage gives ample direct exposure at the level desired. In those few cases approaching, or at least in which skeletal growth has been rapid, however,

better exposure may be obtained by placing the incision in the second interspace. The decision as to where the incision should be placed is best made after study of an anteroposterior roentgenogram of the chest centered over the third rib anteriorly.

*Technique*—The dissection and exposure of the pulmonary artery can be greatly facilitated and accomplished with practically no blood loss if the operator is careful to define and penetrate first a loosely but loosely attached fascial sheath external to which lie all the subpleural collateral vessels. In many cases of pulmonary tenosis, these vessels over the hilus of the lung are engorged and enlarged so that in some instances the appearance of a hemangioma is closely simulated.

Time spent in meticulously cleaning off all the areolar and entinous tissue from the cut end of the systemic artery chosen for anastomosis is well worth while. If this is not done, strands of the tissue adhere to the anastomotic suture and are herniated through the needle holes into the lumen of the artery. A less diligent excision of adventitious tissue has been employed in preparing the pulmonary artery at the site chosen for anastomosis because of the thinness of the wall of this blood vessel.

The incision into the lumen of the pulmonary artery as Blalock has indicated should always be made transversely to the axis of the artery. In our experience a better anastomosis results if the incision is placed definitely on the cephalad surface of the vessel. For this purpose a sharp dissection scissors with small blades has been found best. If an opening is made first which appears to be smaller than is actually needed and the posterior row of the anastomosis put in, the operator often finds that the small opening, through traction and manipulation, has increased to an adequate size. If this is not the case, the opening can easily be enlarged during the formation of the anterior row of the anastomosis by an additional small snip of the scissors. Unless great care is taken there is much more likelihood of making the initial opening in the pulmonary artery too large rather than too small.

The principles developed and recommended by Blalock for the technical construction of the anastomosis were followed with only minor variations. Ethicon silk sutures 00000 or 000000 double armed with three-eighths curved half needles proved very satisfactory. A continuous or *g* mattress suture was employed in most cases for the entire anastomosis. In a few patients, however, the anterior row was completed with an ordinary whipping stitch. The operator must constantly guard against puckering of the wall of the systemic artery and the resulting formation of constricted areas. This is best avoided by placing the posterior row of the suture loosely before pulling it up and approximating the two blood vessels. Separate interrupted sutures should then be placed and tied at either end of the posterior row. Gentle traction on these stay sutures while the anterior row is being completed will ensure a wide stoma.

Most of the anastomoses leaked a few cubic centimeters of blood when the clamps were removed. Usually this ceased within a minute or two if light

pressure with a sponge or cottonoid pledget was made over the suture line. Perforating leakage was controlled with an additional interrupted suture or two. Fortunately we have never had to contend with leakage from the posterior side of the anastomosis. The clamps on the pulmonary artery should be removed first and then after two or three minutes the clamp on the systemic artery.

**Anesthesia.**—The importance of an excellently administered anesthetic for the successful surgical treatment of a patient with pulmonary stenosis cannot be overestimated. The two things to be feared most from the anesthetic standpoint are (1) that the patient will not receive sufficient oxygen during the operation thus causing immediate death or permanent brain damage and (2) cardiac arrhythmia or cardiac standstill. It is not meant to imply that either of these things is entirely within the control of the anesthetist. The surgeon must also bear his share of the responsibility but a major portion of the anesthetist's attention must be centered on these points. Only by close harmonious teamwork between surgeon and anesthetist can the best results be obtained.

The necessity of maintaining an open airway at all times dictates the routine use of a small fitting intratracheal tube. In the larger children tubes with a surrounding balloon cuff can be safely used but in smaller children and especially in those patients under 4 years of age we have felt that a plain tube without inflatable cuff was less apt to damage the mucosa of the larynx and produce postoperative edema.

To insure that the patient receives the maximum amount of oxygen during the operation the anesthetist should not allow or the surgeon demand, that the lung in the pleural cavity through which the operation is performed be completely collapsed at any time. If 10 to 15 cm. of water pressure are maintained in the trachea by the anesthetist the lung will remain inflated except for a small portion of the upper lobe which, by necessity, will be compressed by the surgeon. In our opinion the normal situation should be that the surgeon is continually fighting the lung. This is not difficult since once the chest is opened the exposure required for the remainder of the operation is not great.

The first patients in this series were operated upon with cyclopropane as the anesthetic agent. With this gas, the patient can be given 90 per cent oxygen and in some cases it seemed the ideal anesthetic agent. However, in those patients who develop cardiac irregularities, one hesitates to continue the administration of cyclopropane and wonders whether or not certain effects of the gas have not produced the irregularities. For this reason a mixture of 1 per cent of thal and curare in the proportion of 1 mg. of penthal and 5 units of tubocurarine per cubic centimeter (Baird solution) injected 1 cm. while 100 per cent oxygen was administered through the intratracheal tube has been employed, with increasing frequency. Expertly given, this combination seems to be the best.

A few patients apparently will die from cardiac failure during the operation no matter what precautions are used to prevent it. Several of our patients developed irregularities of heart rate and in two instances death resulted. One possible cause for these occurrences would seem to be neurogenic reflexes initiated by operative trauma about the hilus of the lung and the reflex of the aorta.

Inasmuch as some of the instances of arrhythmia we observed were accompanied by a slowing and dilatation of the heart it was concluded tentatively that vagal reflexes were probably of significance. Therefore we have made a point of injecting the trunk of the vagus nerve with 1 per cent Novocain solution as soon as it could be exposed just above the hilus of the lung or below the arch of the aorta. This has seemed definitely to minimize irregularities in the heart rate. Intravenous injections of atropine sulfate in relatively large doses during operations have been tried but not with as much effect as the actual blocking of the vagus nerve with Novocain.

*Psychiatric Observation*.—Fifteen patients were tested preoperatively. It was felt that the improved oxygenation of the brain after a successful operation might be reflected by an improvement in the intelligence of the child. The period of time since operation is too short to permit a final evaluation of this possibility but observations up to the present indicate that little if any changes occur. All our children in the group that was examined had above average intelligence quotient prior to operation. A child with pulmonary stenosis often presents a behavior problem which the parents have been reluctant to try to correct, since disciplinary measures frequently provoked crying fits, tantrums, which increased the cyanosis. In addition, these children after a prolonged period of limited physical activity are inclined to be withdrawn and unfamiliar with group activities. These peculiarities of behavior have invariably largely disappeared soon after operation if a good result was obtained.

*The Eisenmenger Complex*.—One patient 36 years old, not included in the present series, was operated upon. In the past at the presence of an Eisenmenger complex was strongly suspected. Operation was finally agreed to upon the patient's own insistence and because in our minds, the presence of a pulmonary stenosis could not be entirely excluded.

This patient had been cyanotic since birth and had always noted moderate dyspnea on mild physical exertion but had been able to work steadily during World War II as an electrician in a shipyard.

Physical examination revealed marked cyanosis at rest with definite clubbing of the fingers and toes. The heart was considerably enlarged. A murmur could be heard. Blood pressure was 160/13. Roentgenologic studies revealed enlargement of both ventricles and the pulmonary cones. Vascular markings were increased in both lung fields. The hilus of the right lung showed no pulsation, but definite pulsation was seen at the hilus of the left lung. The fluoroscopy showed right axis deviation. Blood studies revealed the following: hematocrit, 77 per cent; hemoglobin, 20 Gm.; red blood cells, 10,200,000; oxygen saturation of arterial blood, 62 per cent; oxygen content, 17.9; oxygen capacity, 28.6.

Exploration was made through the left side of the chest. There were an unusual number of lateral blood vessels coursing into the lung beneath the pleural reflexion at the hilus. When exposed, the left pulmonary artery measured one inch in diameter. It was thick-walled and had the grumpy appearance

of the aorta. A needle attached to a water type manometer capable of measuring pressure up to 50 cm. of water was inserted into a branch of this huge vessel. The pressure within could not be measured however since the fluid in the manometer was immediately shot out at the top. This appeared to confirm our preoperative impression that this patient had an Eisenmenger complex.

The chest was closed and the patient was returned to his room in good condition. Two hours after operation as the nurses were turning the patient in bed he suddenly gasped and died within a few seconds.

At autopsy the typical findings of the Eisenmenger complex were demonstrated. There was no pulmonary stenosis, but rather a tremendous dilatation of the pulmonary artery and its branches. The walls of all these vessels were increased in thickness comparable to systemic arteries. The pulmonary artery measured 10 cm. in circumference at autopsy. The right pulmonary artery was almost occluded by an old organized thrombus and the left was partially occluded by a recent ante-mortem thrombus which was thought to be an embolus. The origin of the embolus was not determined.

#### SUMMARY

The results obtained in the surgical treatment of forty-three patients with pulmonary stenosis are reported. Six patients died five during operation or in the immediate postoperative period and on six weeks after discharge from the hospital. The causes of death are discussed. An anastomosis was made between the innominate artery and a pulmonary artery in three instances and between a subclavian artery and a pulmonary artery in thirty-seven instances. An improvement was observed in four patients following operation due to the formation of thrombi at or adjacent to the vascular anastomosis. The most frequent postoperative complications were (1) pleural effusion (2) hemothorax (3) brain damage from relative anoxemia. The method of approach and choice of the systemic vessel to be used for the anastomosis are discussed. In our opinion most cases are best treated by making an anastomosis between the left subclavian artery and the left pulmonary artery. Certain aspects of operative technique and anesthesia are discussed. Experience with one patient having the Eisenmenger complex is related.

#### CONCLUSIONS

1. The surgical treatment of patients with pulmonary stenosis gives the best result if the care of these patients is supervised by a team of doctors especially interested in the problem.

\* An anastomosis between a pulmonary artery and the innominate or subclavian artery should benefit 75 per cent or more of such patients. The mortality of such an operation should be 14 per cent or less.

2. In all patients in whom the preoperative arterial oxygen saturation is less than 60 per cent the approach should be through the left side of the chest and the subclavian artery should be used for the anastomosis, whether the aorta arches to the right or to the left.

Inasmuch as some of the instances of arrhythmia we observed were accompanied by a slowing and dilatation of the heart it was concluded tentatively that vagal reflexes were probably of significance. Therefore we have made a point of injecting the trunk of the vagus nerve with 1 per cent Novocain solution as soon as it could be exposed just above the hilum of the lung or below the arch of the aorta. This has seemed definitely to minimize irregularities in the heart rate. Intravenous injections of atropine sulfate in relatively large doses during operations have been tried but not with as much effect as the actual blocking of the vagus nerve with Novocain.

*Psychiatric Observations*.—Fifteen patients were tested psychometrically. It was felt that the improved oxygenation of the brain after a successful operation might be reflected by an improvement in the intelligence of the child. The period of time since operation is too short to permit a final evaluation of this possibility but observations up to this present indicate that little if any change has occurred. Many children in the group that was examined had low average intelligence quotients prior to operation. A child with pulmonary stenosis often presents a behavior problem which the parent has been reluctant to try to correct, since disciplinary measures frequently provoked crying or tantrums, which increased the cyanosis. In addition these children after a prolonged period of limited physical activity are inclined to be withdrawn and unfamiliar with group activities. These peculiarities of behavior have invariably largely disappeared soon after operation if a good result was obtained.

*The Elongate Complex*.—One patient 38 years old, not included in the present series, was operated upon. In this patient the presence of an Eisenmenger complex was strongly suspected. Operation was finally agreed to upon the patient's own insistence and because in our minds, the presence of a pulmonary stenosis could not be entirely excluded.

This patient had been cyanotic since birth and had always noted moderate dyspnea on mild physical exertion but had been able to work steadily during World War II as an electrician in a shipyard.

Physical examination revealed marked cyanosis at rest, with definite clubbing of the fingers and toes. The heart was on a laterally enlarged. A murmur could be heard. Blood pressure was 100/135. Roentgenologic studies revealed enlargement of both ventricles and the pulmonary conus. Vascular markings were increased in both lung fields. The hilum of the right lung showed no pulsation, but definite pulsation was seen at the hilum of the left lung. The electrocardiogram showed right axis deviation. Blood studies revealed the following: hematocrit 77 per cent, hemoglobin, 20 Gm., red blood cells, 10,200,000, oxygen saturation of arterial blood 67.5 per cent, oxygen content 17.9 cc. per cent,  $\text{pO}_2$  28.6.

Exploration was made through the left side of the chest. There were an unusual number of collateral blood vessels coursing into the lung beneath the pleural reflex on at the hilum. When exposed the left pulmonary artery measured one inch in diameter. It was thick walled and had the gross appearance

of the aorta. A needle attached to a water type manometer capable of measuring pressures up to 50 cm. of water was inserted into a branch of this huge vessel. The pressure within could not be measured, however, since the fluid in the manometer was immediately shot out at the top. This appeared to confirm our preoperative impression that this patient had an Eisenmenger complex.

The chest was closed and the patient was returned to his room in good condition. Ten hours after operation, as the nurses were turning the patient on his back, he suddenly gasped and died within a few seconds.

At autopsy the typical findings of the Eisenmenger complex were demonstrated. There was no pulmonary stenosis, but rather a tremendous dilatation of the pulmonary artery and its branches. The walls of all these vessels were increased in thickness comparable to systemic arteries. The pulmonary artery measured 10.5 cm. in circumference at autopsy. The right pulmonary artery was almost occluded by an old organized thrombus and the left was partially occluded by a recent ant-mortem thrombus which was thought to be an embolus. The origin of this embolus was not determined.

#### SUMMARY

The results obtained in the surgical treatment of forty-three patients with pulmonary stenosis are reported. Six patients died, five during operation or in the immediate postoperative period, and one six weeks after discharge from the hospital. The causes of death are discussed. In anastomosis was made between the innominate artery and a pulmonary artery in three instances, and between a subclavian artery and a pulmonary artery in thirty-seven instances. No improvement was observed in four patients following operation due to the formation of thrombi at or adjacent to the vascular anastomosis. The most frequent postoperative complications were (1) pleural effusion, (2) chylothorax, and (3) brain damage from relative anoxemia. The method of approach and choice of the systemic vessel to be used for the anastomosis are discussed. In our opinion most cases are best treated by making an anastomosis between the left subclavian artery and the left pulmonary artery. Certain aspects of operative technique and anesthesia are discussed. Experience with one patient having the Eisenmenger complex is related.

#### CONCLUSIONS

1. The surgical treatment of patients with pulmonary stenosis gives the best results if the care of these patients is supervised by a team of doctors, especially interested in the problem.

2. In anastomosis between a pulmonary artery and the innominate subclavian artery should exceed 70 per cent or more of such patients. The mortality of such an operation should be 14 per cent or less.

3. In a patient in whom the preoperative arterial oxygen saturation is over 50 per cent the approach should be through the left side of the chest and the subclavian artery should be used for the anastomosis, whether the aorta lies to the right or to the left.



4 The intravenous injection of a mixture of pentothal and curare in the proportion of 25 mg. of pentothal to 5 units of tubocurarine per cubic centimeter (Baird's solution) is the best type of anesthesia

5 Cardiac irregularities during operation are decreased if the vagus nerve is blocked with Novocain as soon as possible after the chest is opened

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## PULMONARY DECORTICATION IN THE TREATMENT OF EARLY PYOGENIC EMPYEMA

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THE purpose of this article is to present the rationale for the use of pulmonary decortication in the treatment of selected cases of early empyema and to cite the results obtained in a small series of five cases so treated.

After our experiences with the use of pulmonary decortication in cases of massive early empyema complicating hemothorax following penetrating and perforating wounds of the thorax,<sup>1</sup> we became interested in the feasibility of its successful application to cases of early empyema unassociated with intra-thoracic wounds.

On reviewing the literature it is found that since DeLorme and Fowler first performed decortication of the lung for chronic empyema the use of the operation has been limited almost entirely to the treatment of the disease in its late phase. On reviewing thirteen of the most commonly used textbooks of modern surgery and peritoneal technique its possible successful use in the treatment of acute empyema is not mentioned. However, Lilienthal, for the first time in 1916 advocated its use in selected cases, and did what he called a "major thoracotomy" (mobilization of the lung) as the primary operation in patients not too desperately ill. In others, the major thoracotomy was deferred until after drainage was instituted for immediate relief. In a series of twenty-three cases, the results were most encouraging. Although the mortality was 17 per cent, he was convinced of the soundness of the idea of mobilizing the lung early and thereby obviating the possible need for subsequent thoracoplasties for chronicity. Since that time the subject has been given scant attention.

### PATHOLOGY

The rationale of the operation is based on the pathologic changes in the pleural cavity and on the presence of a normally expansible lung or one that can be made so.

The essential pathology of empyema may be summarized briefly. In addition to the presence of pus in the pleural cavity there are six features of major importance:

1. There is a deposition of fibrin on the pleural surfaces in contact with the fluid early in the course of the disease.

Frequently the patches of fibrin coalesce to form a continuous sheet also continuous at the sites of reflection from one pleural surface with another so that the empyema becomes encapsulated.

<sup>Read</sup>  
May 21, 1931. The meeting of the Society of Early City Surgeons, New Orleans, La., U. S. A.

3 The capsule of fibrin begins to be organized early in the course of the disease.

4 That portion of the capsule which overlies the visceral pleura may prevent or markedly retard expansion of the lung.

5 In the early stages of the disease there exists a line of cleavage between the capsule and the pleura.

6 While there exists a line of cleavage between the organizing fibrinous capsule of the empyema and the pleura on which it lies, the pleura remains grossly normal and does not become thickened.

On reviewing nine of the most commonly used textbooks on pathology the last two points cited are not mentioned. On reviewing the thirteen textbooks of surgery and operative technique mentioned previously the last two points cited are also not mentioned. Their recognition is only implied in two books, "one of which refers to Hedblom's statement" that in chronic empyema there is a fibrous membrane (i.e., ours) the pleura, fixing the lung in a partially collapsed condition.

Obviously to decorticate the lung successfully the last two features of the pathology of empyema must be true. The existence of the line of cleavage is mandatory. When a line of cleavage no longer exists, the empyema has ceased to be early and has become later or chronic in the true pathological sense of the term. In the writings on the operation of decortication, the use of the word is deprecated by many authors, and instead the term visceral pleurectomy is substituted. Actually in performing decortication for early empyema the use of the word is exactly descriptive. It is only in the pathologically late cases where the capsule has become fixed with the visceral pleura in the process of organization that it is necessary to perform a visceral pleurectomy in order to obtain expansion of the lung.

That the pleura is grossly normal rather than thickened or fibrotic after pulmonary decortication for early empyema we have seen repeatedly at autopsy. That this condition must be present in order to obtain immediate normal pulmonary expansion is obvious. Otherwise a fibrotic visceral pleura could restrict expansion of the lung.

However these two conditions, the existence of a line of cleavage and the existence of a normal visceral pleura beneath the organizing capsule after its removal, are only two of the three conditions which must hold in order to justify decortication. The third condition which must be present is normally expandible lung beneath. It is apparent that the lung must be solely telescopic and capable of expansion. Or if not so, it must not be altered in structure so extensively that one cannot make it capable of expansion. To accomplish this may require the removal and suture of bronchopleural fistula, or even of small lung abscess. It cannot be accomplished when interlobular fibrosis has occurred.

#### DISCUSSION

In the treatment of empyema this problem is solved that of dead space existing in the pleural cavity. It should be needless to say that obliteration of

this dead space is mandatory in order to cure the empyema. It follows that the purpose of deortification in the treatment of early empyema is the rapid obliteration of the dead space by obtaining at operation immediate complete pulmonary expansion. Operating in the presence of gross pus, even though bacteriologically sterile in some cases, the empyema is almost certain to recur if the dead space remains postoperatively.

The indication for the use of pulmonary deortification without preliminary drainage in the treatment of early empyema is considered to be the presence of a cavity of massive size particularly if the collapse of the lung involves the apex. A cavity of massive size is defined as one involving a 50 per cent or greater degree of collapse of the lung.

In the presence of a cavity of such size provided the patient is not too sick to withstand the operation and provided that there is reason to believe the atelectatic lung secondarily collapsed by the empyema has returned to normal otherwise and therefore has regained normal absorptibility or that its absorptibility can be restored at operation we believe that pulmonary deortification without preliminary drainage (primary deortification) may be the treatment of choice for the following reasons:

1 To render negligible or lessen the duration of pleural suppuration.

To restore the function of the lung.

3 To obviolate the possibility of the development of late empyema.

In evaluating the severity of the systemic reaction of the patient to the acute pleural infection the degree of fever manifested is, of course, a valuable criterion. However, it is of lesser importance than the general appearance of the patient, the alertness, the appetite and the response to transfusions. Fever precipitated by a high a 100.0 or 103.0 F body is not considered a contraindication if the patient does not appear too toxic.

Even so, there are patients in whom primary deortification would be indicated on the basis of the size of the cavity but upon whom the operation is contraindicated because of the severity of the illness. If after treatment of such cases by adequate rib resection drainage the lung fails to show satisfactory expansive expansion and the efferection in the size of the empyema cavity at the end of four weeks, deortification of the lung is contraindicated while the empyema is still early. Deortification on these postponed in the presence of a adequate drainage is hereafter referred to as secondary deortification. Secondary deortification is considered indicated in such cases for the same reasons as those enumerated under the aim of primary deortification. The reasoning is based upon the fact that in the

presence of the lung is going to expand satisfactorily after adequate rib resection. It is age so that it appears that the empyema cavity will be obliterated or reduced to a minimum in within a few weeks, it will show a spontaneous union with the pleural space within a few weeks after adequate drainage in the great majority of cases.

Except in the first of the five cases reported here decortication of the lung has not been undertaken by us in the treatment of early empyema with cavities involving less than a 50 per cent collapse of the lung, especially those primarily basal in location, for technical reasons. In performing decortication, it is important that all lobes be freed entirely circumferentially. In our experience including the operations for empyema following intrathoracic wounds and so called hemithorax without empyema<sup>2</sup> it has been rare indeed that the collapse involved a single lobe of the lung or if so that the exposure of the pleural cavity could be limited to that corresponding to a single lobe. Therefore in the event of recurrence of the empyema after decortication for small cavities, it is entirely possible that the extent of the pleural cavity involved in the recurrence would be greater than that for which the operation was undertaken.

The optimum time at which primary decortication should be performed, from a pleural pathologic standpoint is considered to be within six weeks of the onset of the empyema, and preferably as soon as the diagnosis is established with the all chance of several days or more for adequate preoperative preparation. The optimum time for the performance of secondary decortication is approximately four to five weeks after the establishment of adequate rib resection drainage and also within six to eight weeks of the onset of the empyema. These opinions are based on observations of the pathologic changes in the pleural cavity in empyema following intrathoracic wounds. Since each of the five patients reported herein was operated upon within 100 days of the presumed or actual onset of the empyema we are not certain of the exact time limit within which the operations may be performed. That remains to be determined in cases of early empyema associated with intrathoracic wounds. But one might expect that the time limit would be variable dependent upon local conditions and the pathogenesis of the empyema, the virulence of the bacteria, and the resistance of the host.

From a pulmonary pathologic standpoint in the absence of a broncho-pleural fistula or of a communicating lung abscess, the performance of operation must be predicated upon the return of normal expansibility of the empyema is secondary to pulmonary disease such as pneumonia or infarction. If the empyema arises as a primary suppurative pleuritis, as of other extrapulmonary origin, such as the rupture of a subphrenic abscess through the diaphragm, the normalcy of the lung in all respects except for secondary collapse may be assumed. If the complication of lung fistula or abscess is present decortication in the presence of either must be combined with their successful eradication at the time and upon the restoration of normal expansibility thereby.

The technique of the operation in its essential details has been described elsewhere. However two features of the procedure postoperative care should be stressed. These two features are drainage and antibiotic therapy.

The maintenance of complete pulmonary expansion in adequate postoperative closed drainage of the pleural cavity is equally as important as the operation. The persistence of dead space in the form of hemothorax or pneumothorax must be avoided.

The role of antibiotic therapy as an adjunct to operation, while difficult to assess in statistical terms, we believe to be an exceedingly important one. In particular the ability of penicillin to prevent or inhibit invasive infection in a high percentage of cases has determined its selection as the agent of choice in these cases at present. The drug has been given in dosages of 25,000 units intramuscularly every three hours for one or two days preoperatively and for seven to fourteen days postoperatively.

That early pulmonary decortication may be accomplished successfully with and without preliminary drainage in selected cases of early empyema, safely and with resulting cure or marked improvement in far less time than by the conventional method of rib resection drainage alone, is attested by the accompanying case reports. The main features of the cases are presented in Table I and the detailed report follows.

It is important to note that the discussion of the pathology of empyema presents no new observations. The fundamental features of the anatomic and physiologic pathology of empyema remain the same as when they were first clearly established by Graham<sup>1</sup> and his associates. As a result of that work, the principles of the treatment of acute or early empyema were placed upon a sound basis for the first time.

Among the essential observations on the treatment of empyema made by Graham at that time were the following:

1. Open pneumothorax must be avoided in the acute stage of the disease. Comparatively little danger is to be feared from an open operation after the acute stage of the disease has passed.
2. The prevention of chronic empyema must be accomplished by the rapid sterilization and obliteration of the infected cavity.

In the series of cases reported herein these principles were adhered to in that at the time of primary or secondary decortication the pneumonic or other etiologic pulmonary disease had subsided. The dangers of open pneumothorax were minimized by the use of positive pressure anesthesia, obliteration of the cavity was obtained by decortication and postoperative drainage and sterilization of any residual cavity was attempted by the use of penicillin parenterally and locally in the pleural space.

#### CASE REPORTS

Case 1—J. E. C., 31 years of age, sergeant in the Army of the U. S., aged 33 years, admitted to the 300th General Hospital at Viterbo, Italy, Jan. 20, 1944. For the three months previous he had pains in the left lower part of the chest. On Jan. 14 he began to feel fever (101 F), chilly sensations, and shaking of the arms and legs. Three days later he began to feel pneumonia and frequent urination. In addition, he experienced a constant low backache developed cough productive of mucus, black sputum and pain of pleuritic character in the left lower thorax. For the next five days prior to admission he was in the hospital. The chest examination disclosed no definite disease.

On physical examination the temperature was 99.4° F, pulse 90 respirations per minute and mucous membranes were pale and the patient appeared bronchial. On



the left lower lung posteriorly the pericardium and was impaired and the breath sounds were suppressed. There were no rales. The remainder of the examination was negative.

On admission, the result of the laboratory examination was as follows: red blood cells, 4,000,000; hemoglobin, 90 per cent; white blood cells, 17,900; polymorphs, 65 per cent; eosinophiles, 4 per cent; lymphocytes, 25 per cent; analysis normal.

A roentgenogram of the thorax on admission was reported as showing typical pneumonia in the left lower lobe.

On this basis the diagnosis of typical pneumonia was made.

From the time of admission until June 7, 1944, he had fever each day with temperature up to 101° and 102° F. During this period from May 7 to June 6, he was treated with sulfadiazine 1.0 Gm. every four hours. Because of the possible development of empyema, thoracentesis on the left lower lobe was performed May 29, 1944, and a nonproduct of fluid. But on May 31, 1944, 50 c. of bloody rather thick fluid were withdrawn. On this latter date, roentgenogram, the entire left lung field was filled with moderately dense homogeneous shadow.

From June 6 to July 15, 1944, the temperature did not rise above 100° F. On June 14, 1944, another roentgenogram of the chest showed encapsulated fluid in the lower half of the left lung and three days later thoracentesis in this region was productive of 40 c. of thick sanguinolent fluid. On July 1, 1944, 25 c. of thick grayish brown pus were aspirated on thoracentesis in this region and on July 5, 1944, 60 c. of similar pus were aspirated. Thereafter from July 7 through July 13, daily thoracentesis performed with withdrawal of pus in amount varying from 5 to 70 c. and each withdrawal after treatment with 1,000,000 units of penicillin in 5 c. of saline solution resulted in the pleural cavity. During this time moderate leucocytes persisted. A roentgenogram of the chest showed no significant change in the size of the empyema cavity. On four occasions, aerobic and both aerobic and anaerobic cultures of the pleural pus failed to demonstrate the presence of any bacteria. A guinea pig inoculated with the pus during this time was reported later as failing to develop disease following intraperitoneal injection.

Because of persistence of the empyema in spite of local penicillin therapy, open thoracic drainage was performed July 13, 1944, by partial resection of the eighth rib in the post axillary line. The cavity found occupied primarily the paravertebral gutter and contained large masses of fibrin. After insertion of large thoracotomy tube the wound was left open.

The course was uneventful until one day after the rib resection drainage began the patient began to have temperature as high as 104° F. which fever persisted for five days. During this febrile period, no immediate cause was found other than a cut upper respiratory infection. However, after the development of bronchopneumonia distal to the end of this brief period he fever subsided. Thereafter the bronchopneumonia distal lowered spontaneously because no further subsequent operation. From the date of onset of the fever, July 24, 1944, systemic penicillin was administered in dosages of 12,000 units every three hours for the next eleven days, the total dosage being 1,320,000 units.

In the next week there was no diminution in the size of the cavity. It was still capable of only 65 c. but on digital examination it seemed to have increased in size at the time of the rib resection drainage. Three months of persistent drainage by thoracic drainage had no apparent decrease in the size of the cavity. Second thoracotomy for decortication of the lung with pre and postoperative systemic penicillin therapy adjunct, was decided upon.

Accordingly on July 15, 1944, twenty-eight days after the onset of the pneumonia, under tracheal ether anesthesia the left pleural cavity was entered through posterolateral rib incision. The fourth intercostal space without rib section was resected. On opening the parietal pleura and spreading the rib, the cavity was found to be large and the entire part of the inferior part of the posterolateral surface of the upper lobe and the entire posterolateral surface of the lower lobe. Prior to decortication, the lower lobe was about 20 per



vent collapsed, and the lobe would expand under positive pressure. From the 12 o'clock position of each lobe dense fibrous layers about 3 mm. thick were removed, exposing beneath gross normal visceral pleura. Several small incisions made in the visceral pleura were closed with interrupted silk sutures. The entire lobes were freed entirely of adhesions by breaking with the sweep of the hand any fibrous adhesions between the lobes or the pleura in the portions of the pleural cavity not occupied by the empyem. Following the under positive pressure both lobes expanded completely into the pleural cavity. That portion of the fibrous capsule covering the parietal pleura was not removed. It did not have any effect on the expansibility of the lung. Internal intercostal nerve block as performed with 1 per cent Novocain. Penicillin, 50,000 units 100 mg. normal saline solution was placed in the pleural cavity. Intercostal tubes were brought out in the second and fifth interspaces (external) and the eighth interspace in the posterior axillary line. The wound was closed without drainage. The two pericostal silk sutures and the chest wall were closed with interrupted cotton sutures throughout. During operation, 2000 cc. of citrated blood and 2000 cc. of glucose (5 per cent solution) in normal saline solution were administered, although shock did not occur. Following operation, bronchography was performed. Also following operation, the intercostal tubes were opened under tension for closed drainage except the opening of the eighth interspace tube was closed for six hours to prevent the prior escape of the penicillin.

A culture of the pleural pus obtained at the time of decortication reported as positive for *Staphylococcus aureus hemolyticus*.

There were no immediate postoperative complications except pyrexia which appeared 12 hours after the day of operation, the subsequent rise of the temperature to 59°. The pyrexia disappeared completely the next few weeks. There were no other manifest signs of toxic reaction. The temperature rose to 100° F. on the day of operation, fell slowly to become normal on the fourth postoperative day and remained so thereafter. The wound healed promptly without apparent infection. The two antiseptically placed intercostal tubes were removed on the seventh postoperative day and the remaining intercostal tube was removed on the thirteenth postoperative day. At no time was there persistent drainage. Penicillin in dosages of 3,000 units every three hours as directed was used on the sixteenth postoperative day, total of 3,400,000 units being administered for the previous eighteen days. Also on the sixteenth postoperative day the patient completely ambulatory again.

On Sept. 2, 1944  
in regard to the  
possibility of fluid  
nonproductivity of fluid  
and no fluid  
counters

per cent solution) as performed, followed by relief of left thoracic pain experienced since the onset of the last episode of fever. On Sept. 14, 1944, small abscesses in the left thoracotomy scar ruptured spontaneously draining small amount of gray pus. Cultures of this pus yielded the presence of *Staphylococcus aureus* (nonhemolytic) and *Gramella streptococcus*. The patient continued febrile and ambulatory for the remainder of the hospital stay but draining abscess in the wound persisted. A communication with the pleural cavity could never be found, although the possibility could not be excluded. The patient returned to the United States Sept. 20, 1944, for further observation.

A letter from the patient was received several months later in which he stated that another operation had been performed soon after his return, because of the draining abscess. He stated also that empyema not found, but tentative opinion is not advisable and his subsequent course could not be ascertained.

Comment.—The operation of secondary decortication was undertaken in this patient because of lack of any expansion of the lung after adequate drainage of the empyema had existed for one month, and the fact that chronic empyema

was impending. Although the operation was not definitely followed by a prompt cure the patient was considered greatly improved. If the postoperative draining sinus communicated with an empyema cavity the cavity was certainly markedly reduced in size compared to that present at the time of decontamination. For this reason, any subsequent operations becoming necessary would be of far less magnitude than that which would have been necessary had the original cavity persisted into pathologic chronicity.

On May 11, 1944, Corporal the Army, aged 22 years, was admitted to the 300th General Hospital in England on Aug 28, 1944. He had been in a Japanese prisoner of war camp since 1941 which he escaped on May 11 of the right thorax. Following the incident he was admitted to a British military clearing station, where he was found to have multiple fractures of the third rib and of the scapula. A crossosternal incision was made on the left side. There was a wound of the thoracic wall. The costal thorax was closed on the right with drainage of blood being removed, after which 30,000 units of penicillin was injected into the pleural cavity. He was transferred to United States General Hospital, where he remained until he was discharged on November 1944. At the first General Hospital, thoracotomy on the right was done Aug 1944 and 75 cc of blood fluid was removed. No further history was obtainable.

On examination on admission, the temperature was 101°F, the pulse 118, and the respirations 18. The patient appeared to be well and seemed to be in good health. A occasional cough produced a few sputa. There was no dyspnea. The right side of the thorax showed marked crepitation and limited expansion. The heart and left lung were normal. Over the right lung base extending into the axilla the percussion note was dull and the breath sounds were absent. There was marked prominence over the lateral side of the right scapula and bulging of the right chest was limited to 30 degrees.

Laboratory and roentgen examination revealed the following: (a) blood cells, 27 polymorphonuclears, 77 per cent eosinophils, 1 per cent lymphocytes, 3 per cent monocytes, 13.5 (100 volume packed red blood cells), 30 per cent total plasma proteins, 22 (100 volume packed red blood cells). (b) roentgenogram of the thorax showed a old, complex, communicating fracture of the posterior portion of the right third rib, and of the superior border of the second process of the right scapula. A large localized hydropneumothorax was present on the right, the complete collapse of the lung.

On Aug 30, 1944, there were scars on the right chest (three sites posteriorly) which were (a) few red scars, (b) moderate scars, (c) large scars. (d) being scars for proteolytic Clostridium welchii infection for 24 hours.

On the basis of his the impression was that total empyema existed on the right representing several hemithoraces. The source of the hemithorax could be from a point in the lung by rib fracture or from tears in the chest wall, or both.

Because of our experience in the history of early pulmonary decontamination in cases of severe empyema following traumatic wounds complicated by hemithorax, we became of the belief that the pleural pathology could differ in that had the patient had a wound of the thorax. He was treated with the rib fracture the method of therapy decided upon as paraffin decontamination with thorax preliminary drainage.

The simple fracture, the crossosternal incision, and the restoration of the function of the scapula by paraffin presented no problems and hence will not be mentioned further.

Between Aug 11 and Sept 1, 1944, the patient was given 100,000 units of intrateal blood serum of anti-paraffin. On the day of admission, penicillin therapy 50,000 units over three hours intramuscularly. Later and it was continued in the postoperative period. The average daily temperature for 10 days was 100.5°F during the week before operation.

On Sept 4 1946 an intratracheal tube was inserted after a midline incision. A right thoracotomy was performed. The pleural cavity was entered in the sixth intercostal space posterolaterally without rib section. A virtually total empyema was found, the cavity containing thick pus and large masses of fibrin. Cultures of the pus were reported positive for proteolytic *Clostridium* and hemolytic *Staphylococcus aureus*. The lung was collapsed into the paravertebral gutter and the apex as down to the level of the fourth rib posteriorly. The diaphragm was high and fixed. The lung was covered by a thick organizing membrane and did not expand under positive pressure. The membrane was readily stripped from the visceral pleura in large sheets. After the thick membrane was removed the lung remained partially collapsed, the visceral pleura still being covered by a very thin transparent fibrous sheet which produced fine blisters of the lung upon itself especially at the free margins of the lobes. After removal of the latter membrane under positive pressure the lung expanded completely. All the bronchovascular structures were preserved. During the dissection, two small lacerations were produced, one in each lobe. These were closed with interrupted fine cotton sutures. An intercostal nerve block was performed using 1 per cent solution of Novocain. The intercostal tube drain was re-brought out the second intercostal space anteriorly. A eighth intercostal space at the posterior axillary line. A 50,000 units of penicillin was given. A normal saline solution was instilled into the pleural cavity. The wound was closed by layers without drainage and without pericostal sutures, with interrupted cotton sutures throughout. During operation, 1,000 cc of citrated blood was given, though shock did not occur. Immediately following operation bronchoscopy was performed and showed drainage of the pleural cavity instituted by opening the intercostal drain under tension. Opening of the eighth interspace drain delayed for six hours to prevent the early escape of penicillin.

Following operation, the temperature rose to 101 F on the same day and thereafter fell gradually to become normal on the third postoperative day. The anterior intercostal drain was removed on the second, and the posterior on the seventh postoperative day. There was no persistent drainage at any time. The wound healed per primam.

On the sixth postoperative day the patient experienced considerable pain in the left side of the chest at this time first on rub as heard only once and never recurred. Because of persistence of the pain, an intercostal nerve block on the left including the third through the twelfth nerves, as performed ten days later using Novocain (1 per cent solution) gave relief of the pain, which did not recur. On each of the two days of pain, the temperature rose to 101 F and then returned to normal again.

Protein penicillin therapy, which was begun on the day of admission, was discontinued on the fourteenth postoperative day the patient having had a total of 4,250,000 units during the previous twenty-one days.

Following the discontinuation of the penicillin therapy, low grade irregular fever occurred, and persisted for ten days. At the end of this time roentgenogram of the thorax showed for the first time small areas of infiltration in the left lower lobe suggestive of bronchopneumonia. Thereafter the patient remained febrile and tachycardic throughout the hospital stay. On two subsequent roentgenograms of the thorax, the left lung field was normal.

For the first several weeks following operation, very small pulmonary nodules on the right, about final level, appeared in the roentgenograms. Throughout the postoperative period of observation, however, the right lung field remained clear and so time as there clinical or roentgenographic evidence of recurrence of the empyema.

**Comment**—In spite of apparent prompt cure of the empyema by primary decortication, the patient failed to regain full strength rapidly and had a persistent tachycardia during normal activity. The total plasma proteins were found low (5.6 Gm per cent) during this period, although the determinations were restored to a normal range (around 7.9 Gm per cent) by blood transfusion.

Soon, there was no significant clinical improvement. Therefore Nov 16 1944 he was returned to the United States for further convalescence because of weak heart and tachycardia.

CASE 2—A 31 aged 39 years, private in the Army of the United States, was admitted to the 200th General Hospital in Naples, Italy in the latter part of October 1944.

On Oct 1 1944 at another U. S. Army General Hospital he had had a perforated ulcer for an acute abdominal illness of eight hours' duration. A perforated gastric ulcer was found at laparotomy a day later. Prior to the acute illness, he had never had any gastric symptoms. The postoperative course was stormy and complicated by left hydrothorax. On three or four occasions between Oct 3 and Oct 8, 1944 blood-stained fluid was removed from the left thorax by thoracentesis. The patient was then transferred to another U. S. Army General Hospital, where on Oct 10 1944 a portion of the left tenth rib was removed for exploration, and open drainage established. The cause of the empyema was considered to be bacterial infection of the rib.

The patient came under our observation for the first time on Oct 30 1944. At this time on examination, the patient appeared only moderately sick. The temperature 99.6 F, the pulse 112, and respirations 20. The heart and right lung are normal. Over the left lateral thorax in the midaxillary line there was fluctuant abscess of the soft tissues about 2 cm. in diameter. There was a large thoracotomy tube for drainage in the left tenth rib defect in the post-ribo-axillary line. The purulent drainage from the thoracotomy tube was foul smelling. No communication existed between the thoracotomy wound and the abscess of the thorax, all superior to it. The empyema cavity as large and empty and a drainage tube adequate. The abdomen was soft. Except for the laparotomy wound which had healed by primary, the abscesses were normal.

Initial laboratory examinations were as follows: Hemoglobin, 14.5 Gm. per cent; serum packed red blood cells, 4.8 per cent; total plasma protein, 7.5 Gm. per cent.

The initial roentgenogram of the thorax showed a defect in the tenth rib posteriorly and actual total collapse of the lung in the empty pleural cavity on the left.

Regarding the gastric ulcer, the patient had symptoms related to it during the hospital stay and no special therapy therefor as directed. X-ray examination of the upper gastro-intestinal tract during his stay in the hospital showed no evidence of the duodenal cap. There was no evidence of the duodenal ulcer. On repeated examination of the roentgenogram, Dec 12, 1944 there was a finding of a high, the lesser curvature of the stomach and the prolonged pylorus.

On Oct 20 1944, the incision of the left thoracic wall was drained through a posteriorly placed incision. It was situated beneath the incision just outside the rib cage. X-ray examination with the pleural cavity was present. The post-operative incision was closed, of which was reported being post-operative for another Streptococcus. The drainage wound was closed.

For the next few days the course was unremarkable. The empyema drainage tube was left in place. The left lung was not expanding and therefore the empyema still virtually full. As a result of the lack of pulmonary expansion, and hence the lack of expanding drainage, bronchostomy of the lung was decided upon.

From penicillin therapy 22,000 units every three hours, as instituted the day before operation.

On Nov 16, 1944 forty-seven days after the previous onset of the postoperative empyema, and a week after the institution of constant drainage of the empyema left thoracotomy performed under retrophrenic ether anesthesia. A general anesthesia was used through the lower of the two wounds, and was maintained as he proceeded for the drainage of the incision of the thoracic wall. The pleural cavity was closed through the intercostal space about 2 cm. anterior to the thoracotomy. A total empyema was found to

lung being fully 80 per cent collapsed, except for small rim of the lateral surface of the upper lobe back adherent to the lateral thoracic wall. There was evidence of the lung under positive pressure. A bronchopulmonary fistula was not present. The lung was covered by organizing fibroepithelial membrane 1 to 4 mm in thickness (Fig. 1, and 2). Decortication performed. The fall case exposing grossly normal in appearance. Following this, under positive pressure the lung expanded 100 per cent. I teroral intercostal vein block of the second through the eleventh series was done using No. 18 (1 per cent solution). I teroral catheter drainage as provided in the second and fifth intercostal spaces. A 1/2 inch rib pre-existing defect. The chest closed with 10 ribs about periodical sutures, with interrupted silk throughout, leaving open only the skin and subcutaneous tissues where the protractor grafting was done. prevent Compatible chest



Fig. 1 (Case 3).—The section shows the full thickness of the organizing capsule covering the portion adherent to the pleura.

indication of the free border. The angiotensin activity had little

blood count was administered during the operation, although shock was not present at any time. Immediately following operation, bronchoscopy was performed. Also, 50,000 units of penicillin in 200 cc. of normal saline solution were instilled into the pleural cavity through the drainage tubes. All drainage was closed and removed except that the opening of the dependent posterior tube was delayed for four hours to prevent the prior escape of the penicillin. A culture from the empyema cavity taken at operation was reported positive for *Staph aureus*.

Following operation, the temperature rose to a peak of 101.5° F on the first postoperative day. Slight jaundice (icteric index 19) developed rapidly and disappeared within the next two weeks. There were no other manifestations of transfusion reaction. By the sixth postoperative day the two anterior intercostal tubes had ceased to function, and were removed. However fever had persisted, with temperatures averaging 102.0° F. At this time

very small locules in the posterior angle of the abscess as found and opened. Culture of the pus from this abscess showed *St. ph. aureus*. On the tenth postoperative day the posterior intercostal tube had ceased to function, and was removed. There was no purulent drainage from any of the intercostal drains at any time. The fever persisted, however. Roentgenograms of the thorax showed complete expansion of the left lung except for residual clouding over the left base. Therefore on Nov. 29, 1944, thoracotomy at five sites was performed, but no fluid was encountered. Ten days later another thoracotomy in the eighth intercostal space in the midscapula line. 10 cc. of bloody pus were removed. Hence on Dec. 3, 1944, the fourteenth postoperative day a section of the left eighth rib was removed at the midscapula line. A very small empyema pocket was entered, which extended as a narrow tract from the region of the healed & formerly placed fifth intercostal space wound down to the healed tenth rib drainage wound. Thoracotomy tubes were placed in the eighth and tenth rib drainage wounds, and open drainage was instituted. Cultures of the pus were positive for *Staphylococcus aureus* and several *Streptococci*.



Fig. 3. — The section shown in Figure 2 has been placed in the deeper or pleural side of the capsule or "bed" (x 250).

The penicillin therapy discontinued on Dec. 7, 1944, the patient having been given total of 3,400,000 units over the previous eighteen days. From Nov. 1, 1944, to Dec. 1, 1944, the patient had received also oral sulfathiazole 10 Gm. four times a day.

Dec. 2, 1944, the temperature which had ranged 104.0 and 110.0 F each day since decortication, returned to normal, and remained so thereafter. The patient further course was entirely unremarkable, and on Dec. 4, 1944, he was returned to the medical floor because of the very small residual empyema and the pleural ulcer.

Comment—Although a very small basal empyema recurred, the patient was considerably improved, the possibility of a massive chronic empyema having been averted by the decortication.

Case 4—C. F. O. aged 20 years, was admitted to the 200th General Hospital, Naples, Italy, June 7, 1943.

April 1, 1943, he was wounded in combat sustaining severe penetrating shell fragment wound of both thighs and of the abdomen. There was no wound of the thorax. After bandaging, laparotomy was done in a forward hospital. Two lacerations of the urinary bladder were found and repaired. There was no diaphragm injury. The wound of both thighs were debrided and closed. Later the wounds of the thighs were secondarily sutured. All wounds healed promptly and the initial recovery was excellent and unremarkable.

On or about May 2, 1943, he developed pleurisy on the left side soon thereafter severe pain in the abdomen. Cultures of the fluid obtained on several thoracenteses soon after the onset were reported sterile. Later he developed pleurisy on the right side also, but without effusion. A pleurisy drippe red shortly and did not recur. A massive effusion on the left persisted. For several days before admission, he had dysuria, and on the day of admission, he was unable to void.

On examination he temperature 99.8 F, pulse 80 and respirations 20. He did not appear ill. The heart and right lung were normal. Over the left lung posteroanteriorly the percussion note was dull and the breath sounds absent. The abdomen pre-tended healed wounds without evidence of major blood vessel, nerve injury or disease. A small stone in the tensor retinaculi just behind the glans penis was palpable. The sexual reflexes were normal.

At the time of the first examination, thoracentesis on the left lateral sites revealed the presence of odorless purulent exudate. A total of 400 cc. of fluid was obtained. The cultures of the pus were reported later sterile.

Initial laboratory and roentgenographic examination were as follows: red blood cells, 4,700,000; hemoglobin, 12 Gm per cent; glucose 90 mg per cent; total red blood cells, 37 per cent; hemoglobin, 11.900; neutrophils, 85 per cent; eosinophils, 6 per cent; lymphocytes, 30 per cent; serum proteins, 3 Gm per cent; urea nitrogen 11.5; but blood cells per high power field, otherwise normal, with no red blood cells present. Roentgenograms of the chest and abdomen showed large hydrothorax present on the left posterior and medial fragments in the right upper quadrant posteriorly. There was marked enlargement of the liver shadow but no shadow suggestive of urinary tract stone.

On admission, the stone in the anterior urethra removed easily. On further study no evidence of additional urinary stones could be found. There are no further urological complications.

The sole problem then remaining was the presence of an abscess in the left side. The bilateral pleurisy and the left empyema, are considered probably secondary to infected pulmonary infection. The plan of treatment decided was pleurotomy, drainage, about preliminary drainage with systemic chemotherapy (adjunct).

Accordingly, on the day before operation, penicillin 400,000 units intramuscularly every three hours was begun. The day before operation 300 cc. of blood was transfused.

June 1, 1943, forty-one days after the onset of the pleurisy on the left, left thoracotomy performed. Each intrathoracic ether anasthesia, through posterolateral incision the pleural cavity entered in the mid intercostal space without central incision in the chest. There was a large empyema cavity situated posteriorly extending from the pericardial diaphragm. The upper lobe including the pericardium collapsed about 25 per cent, and the lower lobe collapsed about 30 per cent. The cavity was filled with foul smelling dark brown pus and large masses of fibrin. A culture of the pus is reported sterile. Part of the capsule of the empyema overlying the diaphragm, which was fixed. The lung could not expand under positive pressure. The lung is then dissected along the visceral portion of the capsule which covered being about 4 mm in thickness. The visceral pleura beneath is grossly normal. There is no bronchopulmonary fistula. One small vein in the lower lobe and in each lobe in the upper lobe produced during decortication, are lined with a thick

ature in each. Following this, there was 100 per cent expansion of both lobes. The diaphragm was freed, reversing its normal motion. No attempt was made to decontaminate the parietal pleura, as the parietal portion of the capsule could have no effect on the expansibility of the lung. Intercostal nerve block of the second through the tenth nerves was performed using Novocain (1 per cent solution). Penicillin, 30,000 units in 200 normal saline solution, was instilled into the pleural cavity. Intercostal tubes for postoperative closed drainage of the pleural cavity were brought out in the second interspace anteriorly and in the eighth interspace in the posterior axillary line. After complete expansion of the lung again under positive pressure the wound was closed in layers with interrupted silk sutures without pericostal sutures. During operation, 1000 cc. of citrated blood and 300 cc. of plasma were administered, though shock did not develop. Following operation, bronchoscopy was performed to clear the tracheobronchial tree of any secretions or blood. The anterior intercostal tube was opened under water immediately following operation. The opening of the posterior tube was delayed for four hours to prevent the prior escape of the penicillin. The patient condition throughout operation good.

Following operation, recovery rapid and uneventful. The temperature rose to a high of 100.0 F. on the night of operation, fell gradually to become normal on the third postoperative day and remained so thereafter. On the second postoperative day the anterior intercostal tube was removed. On the fourth postoperative day the posterior intercostal tube was removed. There was no purulent drainage from either tube. On the fifth postoperative day penicillin therapy was discontinued, the patient having received total of 1,400,000 units over period of seven days. The wound healed by primary. On the eighth postoperative day thoracostomy on the left dry. On the fourteenth postoperative day roentgenogram of the chest showed the left lung to be fully expanded, with no evidence of residual empyema. By this time, he had already become ambulatory. His further course entirely uneventful, and no clinical or roentgenographic evidence of persistence of recurrence of the empyema was detected.

Because the war in Europe already over at this time, on July 4, 1945, he returned to the United States for further convalescence. Although his physical condition was such that he could be served in somewhat duty overseas.

Case 6—W. M. H. (R. par Hospital No. 46561) was hit again, aged 4 years. The patient was admitted on March 26, 1946, with the complaints of pain in the left side of the chest and shortness of breath of several hours duration. He had had cold and cough for two days before admission. Past history was noncontributory.

On examination, there were significant findings except fever, dyspnea, and extra systoles. The heart otherwise normal. Blood pressure was 120/80. The lungs were normal.

Routine blood and urine studies were normal. Blood W. Hermann and Kline negative and blood culture was negative. Blood agglutination versus *Bacterium* and *Proteus* X19 were positive up to 1:50 dilution. An electrocardiogram showed left ventricular preponderance and frequent ventricular premature contractions. A roentgenogram of the chest was not made.

During seven day hospitalization, he had fever with temperatures up to 102.0 F. each day. For the first twenty-four hours, he was given oxygen by intranasal catheter. For two days before discharge he was given sulfadiazine 10 Gm. every four hours.

He was discharged improved April 1, 1946, with the diagnosis of typhus fever.

He was readmitted to the hospital on April 21, 1946, because of continued fever and cough. Also for four days before admission, he had spit up very large amount of purulent sputum day and night.

On examination, the patient was found to be acutely ill, and coughing up thick foul-smelling sputum in frequent intervals. Temperature was 100.4 F. pulse 116 respirations were 34 blood pressure was 120/80. There was dullness, diminished tactile fremitus, and decreased breath sounds over the entire left lung. The right lung normal, heart normal. The remainder of the examination was normal.



All smears examined included the following: Hemoglobin 9.5 Gm; hte blood cells 18,430 polymorphonuclears, 78 per cent; lymphocytes, 20 per cent; monocytes, 2 per cent; urinalysis, normal; total serum protein, 9.44 Gm; albumin, 4.99 Gm; globulin, 4.45 Gm; culture of sputum, *Streptococcus viridans*; blood culture negative. Roentgenogram of the thorax (Fig 4) showed massive hydropneumothorax on the left; the fluid level appeared the first rib anterior; mediastinum displaced to the right, and right lung held near

Three days after drainage 473 cc of foul smelling gray fluid were removed from the left pleural cavity by thoracentesis. The procedure as reported on May 8, 1946, at removal of 150 cc of malodorous pus and 33,000 units of penicillin were instilled in the pleural cavity. The next day 925 cc of pus-like brown pus were removed, and 500,000 units of penicillin instilled in the pleural cavity. Cultures of the pus were positive for alpha streptococcus on each occasion. A smear of the pus was negative for acid fast bacilli. Smears of the sputum on two occasions and culture of the sputum were also negative for acid fast bacilli.



Fig. 4 (Case 1)—Massive hydropneumothorax on the left; fluid level

At this time the patient came under the observation of one of us (H. F. P.). The diagnosis of empyema was expressed on the left, postoperative thoracopleural fistula, was confirmed. Thoracostomy with rib resection drainage as advised. Primary descent of the apex of the extent of the empyema, could have been considered the first of choice but of the following reasons. Temperature was constantly elevated ranging up to 103° F on most days. There was significant tachycardia and tachypnea. The drainage permitted, notwithstanding the blood transfusion. The daily sputum output averaged around 200 cc. The chestal course was not influenced by penicillin, 50,000 units given intramuscularly every three hours beginning on April 29, 1946. It seemed too ill to withstand any further

with five days after the procedure of the most of penicillin  
— five cc  
bilateral

drains as well as visible. A large rubber tube inserted in the wound, and open d. stage initiated. Prophy of the parietal pleura at the time showed nonspecific inflammatory reaction.

Following this, he became febrile promptly. The productive cough practically ceased. He became ambulatory and began to gain weight. In the course of the next few weeks, he given live blood transfusions, 500 each. The anemia disappeared, the hematocrit determination rising to 40 Gm. Postoperative penicillin therapy as before, was discontinued on the twentieth postoperative day.

In July of marked general improvement and the presence of adequate drainage of the empyema, the lung failed to expand fully and bronchopleural fistula remained open. On June 5, 1946, roentgenogram of the thorax, made after the removal of 40 of liquid through the draining tube, showed the empyema cavity shown & that the cavity was well covered (Figs 5 and 6). It involved the posterior half of the left hemithorax. Involvement of the upper and lower lobes and in particular the periphery of the upper lobe collapsed. Recurrent decontamination and wound care continued until chronic empyema was completely



Fig. 5. Case 5.—Residual empyema cavity on the left partially filled with radiopaque oil to show extent.  
Fig. 6 (same case).—After removal of chest drain in July. The empyema cavity is well covered by the posterior half of the pleural cavity.

On June 11, 1946, thoracotomy performed after adequate drainage by rib resection was initiated, and empyema removed. The procedure was performed under total anesthesia either as a thoracotomy or a posterolateral incision. The pleural cavity entered the width of the chest cavity. The lung was removed. On opening the pleural cavity, a large empyema cavity was found. It was in the posterior half of the hemithorax and all of the paravertebral gutter. It extended from the periphery of the lower lobe to the upper lobe. The bronchopleural fistula. Both the upper and lower lobes were collapsed, including the periphery. The collapse of the lung estimated 50 per cent. The empyema cavity also extended

Accessory examinations included the following: Hemoglobin, 9.3 Gm; late blood cells 19,630 polymorphonuclears, 8 per cent lymphocytes, 20 per cent monocytes, per cent erythrocytes, normal; total serum protein 9.49 Gm; lipase, 4.98 Gm; globulin, 4.67 Gm; culture of sputum, *Streptococcus viridans*; blood culture negative. Roentgenogram of the thorax (Fig. 4) showed massive hydropneumothorax on the left (the fluid level appears the first rib anteriorly mediastinum displaced to the right and right lung field clear).

Three days after admission, 473 g of foul smelling gray fluid were removed from the left pleural cavity by thoracentesis. The procedure was repeated on May 3, 1946. It removed 150 g of empysematous pus, and 33,000 cc of pus. It was cultured in the pleural cavity. The next day 925 g of similar brown pus were removed and 700,000 cc of pus. It was cultured in the pleural cavity. Cultures of the pus were positive for alpha streptococcus on each occasion. A smear of the pus negative for acid fast bacilli. Smears of the sputum on two occasions and culture of the sputum were also negative for acid fast bacilli.



Fig. 4 (Case 2).—Massive hydropneumothorax on the left (the fluid level).

At this time the patient came under the observation of one of us (B. F. P.). The diagnosis of acute empyema on the left postoperative (the bronchopleural fistula, as confirmed thoracotomy) with rib resection drainage. Only a primary direct incision over the site of the empyema, could have been considered the treatment of choice for the following reasons: Temperature constantly elevated, ranging from 101.8 F on most days. There was significant tachycardia and tachypnea. The sputum persisted, not diminishing in blood transformation. The daily sputum output averaged around 400 cc. The clinical course not influenced by penicillin, 20,000 units per os intramuscularly every three hours beginning on April 21, 1946. It seemed too late to attempt major thoracotomy.

On May 10, 1946, forty-five days after the previous drainage of the acute empyema, thoracotomy on the left was performed. A massive empyema cavity was found five sub-pleural sections of segment of the sixth rib, in the post-rib area. A bronchopleural

Fig 1

Fig 2



Fig 1

Fig 2

Fig 1 (Case 3) — Transition of increased mass, especially on the left.  
 Fig 2 (Case 5) — Intra projection of chest pleura. In Fig 1 The iron piece to the  
 extent of the exposure on H in the left.  
 Fig 3 (Case 1) — Left as described in section on evidence of exposure.  
 Fig 4 Case 1 — Dissected reveals extensive secondary degeneration in evidence of  
 exposure on the left.

deep into the terlema fissure. The lung was covered by a thin pleural coat to a depth of 3 mm in thickness. It did not expand on positive pressure. Decortication was begun, but was difficult. In some areas, the inflammatory process was found to be pathologically elevated, and therefore visceral pleurectomy was necessary in such areas. The five bronchopulmonary fistulas and several small lacerations produced during the pleurectomy were closed with silk sutures. The lung freed circumferentially. Following this, the lung expanded moderately well under positive pressure but not completely. Over the surface of the lung not involved in the empyema, there was a thick fibrous membrane difficult to remove. An attempt was made to dissect the parietal pleura. The intercostal spaces were irrigated with 1 per cent Novocain solution and 100,000 units of penicillin in 500 cc of normal saline solution were instilled into the pleural cavity. Intercostal catheters for post-operative underwater drainage were placed in the second and fifth interspaces anteriorly and in the

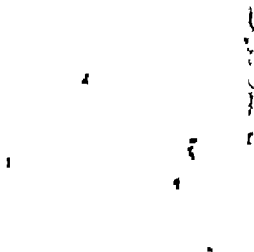


Fig. 7 (Case 8).—The photomicrograph shows fusion between the visceral pleura and the thin coat of the periphery of the lung, indicating pathological chronicity of the empyema in some areas in this case (X 88).

seventh interspaces in the posterior axillary line. After re-exposure of the lung, the major wound closed in layers with interrupted silk, ribbed drainage and chest parietal sutures. The sixth rib drainage wound covered and then closed in similar manner. During the operation, 2,000 cc of citrated blood, 500 cc of plasma, and 1,000 cc of normal saline solution were given intravenously. Bronchoscopy performed after operation. The patient's condition was good throughout, though mild shock was evident at the end. The two anterior intrapleural drains were opened under water immediately following operation. The opening of the posterior drain was delayed for four hours to prevent the juxta escape of pus into the pericardium.

Macroscopic section of the exposed visceral pleural segment of the capsule of the empyema showed an essentially fibrous tissue base covered with granulation tissue. Adjacent to the base in some areas there was collapsed lung tissue showing lymphocytic infiltration (Fig. 7).

Penicillin, 40,000 units every three hours, given intravenously for its effect before secondary debridement and was continued following operation.



Following operation, the temperature rose to  $101.0^{\circ}$  F for the first three days and  $100.0^{\circ}$  F for the succeeding seven days. The patient was out of bed on the second postoperative day. The major thoracotomy wound and the ninth rib drainage wound healed by primary union. The two anterior intrapleural drains were removed on the fourth postoperative day. The remaining drains were removed on the eleventh postoperative day. The drains had been irrigated with penicillin solution infrequently. At no time were there persistent drainage abscesses on the eleventh postoperative day because of local and penicillin therapy. Chest roentgenogram of the thorax at this time indicated persisting fluid in the left base. Thoracentesis was performed at four sites but no fluid was obtained. Chest roentgenogram repeated several days later showed residual pleural pocket containing fluid and air in the left paravertebral gutter to its inferior extent to the level of the sixth interspace (Figs 8 and 9). Thoracentesis at this site produced removal of 50 cc of thick odorless purulent serum. A culture of the pus was positive for nonhemolytic *Staphylococcus aureus*. After several instillations of penicillin solution into the cavity on successive days, there was decrease in the volume. Also the patient tasted the penicillin. Drainage of the small recurrent or persistent empyema cavity in the bronchopleural fistula was indicated.

On July 1946, twenty-one days after the second rib deorientation, short segment of the seventh rib was resected subperiosteally and the empyema was entered. The cavity was small, with an estimated capacity of 50 cc. The bronchopleural fistula was not seen. A large rubber tube was inserted, and open drainage was instituted.

Thereafter his course was unremarkable, and he was discharged from the hospital July 8, 1946.

He returned at intervals to the outpatient clinic for dressings and observation. By August 12, 1946, the bronchopleural fistula had closed; the cavity had been obliterated, and the drainage tube disconnected. By August 27, 1946, the wound had healed completely and the patient was considered well (Fig 10). When last seen on July 6, 1948, there was no clinical or roentgenographic evidence of persistence or recurrence of the empyema (Fig 11).

#### COMMENT

Even though a small empyema requiring secondary drainage followed the deorientation, the patient was considered markedly improved, the possibility of massive chronic empyema having been averted.

#### SUMMARY

1 The rationale of pulmonary deorientation in the treatment of selected cases of early pyogenic empyema is presented.

The pathology of empyema is reviewed, and the rationale based thereon.

3 The indications for primary and secondary deorientation, and the optimum time for rib resection, are given.

4 Five patients so treated are reported upon.

5 In two cases with treatment by primary deorientation, prompt cure of the empyema followed.

6 In three cases with treatment by secondary deorientation, marked improvement followed.

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is also the occasional patient who develops typical lobar pneumonia in the postoperative period but the bronchial type is more common. Many reports<sup>2-5</sup> have indicated that the majority of bacteria found in the upper respiratory tract are susceptible to penicillin and/or streptomycin. By the use of appropriate therapy the quantity of bacteria can be greatly reduced and at times, sterile cultures of sputum can be obtained. It seemed logical therefore to determine by culture the predominant bacteria in the upper respiratory tract of surgical patients before operation and to test the sensitivity of the organisms to penicillin and streptomycin. The number of bacteria can then be reduced by appropriate chemotherapy and the dangers of postoperative pulmonary infection reduced.

It should be emphasized that prophylactic chemotherapy by itself is not the only important feature in a program designed to minimize postoperative pulmonary infection. It must be supplemented by the commonly accepted mechanical measures used to prevent the accumulation of secretions in the tracheobronchial tree and to increase pulmonary ventilation. The patient's airway should be kept free during and after the anesthetic period by tracheal suction and if necessary by bronchoscopic aspiration. During the early postoperative period the patient's position should be changed frequently, he should be encouraged to cough up mucus, and hyperventilation should be carried out with carbon dioxide. Early ambulation should be encouraged and heavy sedation with morphine avoided. The injection of intercostal nerves with local anesthetics such as eucupin in oil will decrease the amount of pain in the upper abdominal and thoracic wound and this method has been used in many of the cases to be reported. These standard prophylactic measures were used in all the patients studied and their pre- and postoperative management differed only in regard to penicillin or streptomycin administered by inhalation. Many patients in both groups also received penicillin by the intramuscular route.

Routine preoperative sputum cultures were made on all patients studied or if no sputum was available the posterior pharynx was cultured. The bacteria were identified by the usual laboratory methods. Penicillin and streptomycin sensitivity was determined by the method of Fleming<sup>6</sup> and patients with more resistant strains of bacteria received larger doses of the chemotherapeutic agent.

#### OPERATION

Preoperative sputum and/or nasopharyngeal cultures were studied in 10 patients (Table I). These patients were for the most part studied during the winter months and *Streptococcus viridans* was found in 183 out of the 19 cases. The other bacteria found are listed and it is noteworthy that *Neisseria catarrhalis* and *Staphylococcus albus* occurred with much higher frequency than the pneumococcus. Nearly all the bacteria encountered were sensitive to penicillin and/or streptomycin.

Forty patients were studied who received penicillin by atomizer (thirty-four cases) or mist (six cases) for two days before and after operation (Table II). This group showed a definite reduction in the number of penicillin-sensitive bacteria present following therapy but there was not the



## INHALATION OF MICROPOWDERED PENICILLIN AND STREPTOMYCIN IN THE PREVENTION OF POSTOPERATIVE PULMONARY INFECTION

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POSTOPERATIVE pulmonary complications present a major hazard in any postoperative patient and they add considerably to the mortality and morbidity of all types of surgery. Pulmonary complications fall into two general groups—those associated with thromboembolism and those related to atelectasis and infection. The embolic complications have been the subject of widespread interest during recent years and it is reasonable to assume that their incidence will be reduced by the judicious use of anticoagulants and prophylactic operation. The prophylaxis of complications associated with pulmonary infection has received little attention although chemotherapeutic agents are now available which when properly used should materially reduce the incidence of postoperative pneumonia. The second type of complication is the subject of this report and is based on our experience during the past year using prophylactic penicillin and streptomycin administered by inhalation in a micropowdered form. This method of administration has been described by Taplin and Bryan and has been found to have definite advantages in postoperative patient. The routine prophylactic use of chemotherapy has reduced our incidence of pneumonia complications in major abdominal and thoracic surgery from the neighborhood of 18 per cent to 1 per cent.

The pathogenesis of postoperative pulmonary infection is probably somewhat different from the typical lobar pneumonia due to a primary infection with the pneumococcus. Postoperative pneumonias are frequently due to bacteria which are considered nonpathogenic in the throat but which become pathogenic in the lung when the normal mechanism of clearing the tracheobronchial tree of secretions is disturbed following an anesthetic. It is quite probable that most postoperative pneumonia begin as small areas of atelectasis due to retained secretion in the bronchi, and these atelectatic areas of the lung are fertile soil for bacteria that under less favorable circumstances would not be virulent. There

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Lederle Laboratories, Inc., supplied the penicillin; Merck & Co., Inc., supplied the streptomycin; and P. H. Le Sue & Company supplied the powdered benzoyl sand in these experiments.

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TABLE III ANALYSIS OF THE BACTERIOLOGIC FLORA BEFORE AND AFTER THE FIRST POSTOPERATIVE PROPHYLAXIS (75 CASES)

ORGANISM	PREOPERATIVE		POSTOPERATIVE
	NUMBER OF	PERCENT SENSITIVE (PER CENT)	NUMBER OF CASES OF INFECTION PRESENT 1 DAY AFTER
<i>Streptococcus</i>			
<i>S. faecalis</i>	5	100	1
<i>S. faecium</i>	4	100	1
<i>S. lactiae</i>	4	35	16
<i>S. coli</i>	7	0	25
<i>S. aureus</i>	10	0	7
<i>S. pneumoniae</i>	4	5	1
<i>S. pyogenes</i>	0		3
<i>S. pyogenes</i>	14	54	4
<i>S. typhimurium</i>	3	0	19
<i>Streptococcus pneumoniae</i>	0		3
<i>S. pyogenes</i>		0	4
<i>S. typhimurium</i>		100	0

Prophylaxis consisted of 1-2 day therapy before and after operation with average of 20,000 units per day.

reduced about equally in the streptococcal and mixed series. It is noteworthy that there was an increased number of cultures positive for *E. coli* after this therapy, but there were no postoperative pulmonary infections which were considered to result from infection with this organism.

Streptomycin was also used in thirty cases pre- and postoperatively and the bacteriologic data are recorded in Table IV. The streptomycin was administered in the micronized form and according to the dosage schedule outlined (Table IV). Streptomycin was also the most commonly encountered organism in this series and it was present in thirty-one out of the forty cases. Postoperatively 17 of the thirty-one positive cases still showed *S. pneumoniae* in spite of

TABLE IV ANALYSIS OF RESULTS FOR PLEURAL FLUID AND PLEURAL TISSUE AFTER STREPTOMYCIN PROPHYLAXIS (40 CASES)

ORGANISM	PREOPERATIVE		POSTOPERATIVE	
	NUMBER OF	PERCENT SENSITIVE (PER CENT)	NUMBER OF	PERCENT SENSITIVE (PER CENT)
<i>Streptococcus</i>				
<i>S. faecalis</i>	11	100	10	30
<i>S. faecium</i>	2	100		
<i>S. lactiae</i>	7	1	1	
<i>S. coli</i>	9	100	1	100
<i>S. aureus</i>	3	100	6	0
<i>S. pneumoniae</i>	1	100		50
<i>S. pyogenes</i>	4	100	7	75
<i>S. pneumoniae</i>	4	100	1	15
<i>S. pneumoniae</i>	1	100		0
<i>S. pneumoniae</i>	1		1	0
<i>S. pneumoniae</i>	1	100	1	0
<i>S. pneumoniae</i>	1	100	0	
<i>S. pneumoniae</i>		1	0	

The lungs received 200,000 units (0.5 gm.) streptomycin (100,000 units the evening before and the morning after) and the pleural cavity was irrigated with 100,000 units the first night and 200,000 units the second night.

The given data are out of 40 cases (25 pre-operative and 15 postoperative) cultures.

TABLE I. MICROORG. FROM CULTURED FROM NASOPHARYNX AND SPUTUM PRIOR TO THYROID (183 CASES)

ORGANISM	PENICILLIN SENSITIVITY		STREPTOCOCCI SENSITIVITY	
	NUMBER OF CASES	% SENSITIVE (PER CENT)	NUMBER OF CASES	% SENSITIVE (PER CENT)
Streptococcus				
St. viridans	151	92	103	91
St. hemolyticus	10	90	10	90
St. absconditus	49	93	14	93
N. catarrhalis	86	31	47	100
Esch. coli	16	0	16	100
H. influenza hemolyticus	30	87	15	100
H. influenza	31	2	—	100
M. phlyoococci				
Staph. aureus hem.	33	85	20	100
Staph. albus	53	47	13	100
Pneumococci	7	100		100
Friedlander bacillus	7	0	3	100
M. tetragenus	6	100	2	100
Yeast	16	21	18	10
Diphtheroids	20	70	3	100
B. proteus	1	0	1	100

postoperative reduction in pulmonary complications that had been expected. We had believed that penicillin given by ordinary throat-spray atomizer would be sufficient to eliminate penicillin-sensitive organisms but there is apparently a need for greater intrapulmonary penetration by the antibiotic. For example, in those patients in whom *St. viridans* were present preoperatively 97 per cent of the organisms were sensitive to penicillin but one-half the patients still had positive cultures postoperatively after specific therapy. A similar series of seventy-five cases is recorded in Table III but the patients were treated with micropulverized penicillin mixtures rather than by the atomized or usual aerosol method. In this series, the *St. viridans* were found to be 100 per cent sensitive preoperatively and no positive culture was found postoperatively after treatment. The number of cultures positive for *St. ph. hemolyticus* was

TABLE II. ANALYSIS OF THE RESPIRATORY FLORA BEFORE AND AFTER THYROIDECTOMY (BY STOMACH, 34 CASES, APRIL 1948)

ORGANISM	BEFORE THYROIDECTOMY		AFTER THYROIDECTOMY	
	NUMBER OF CASES	% SENSITIVE (PER CENT)	NUMBER OF CASES	% SENSITIVE (PER CENT)
Streptococcus				
St. viridans	1	97	1	0
St. hem.	7	100	0	14
N. catarrhalis				
Esch. coli	1		1	1
Staph. albus	4	100	1	1
Staph. aureus hem.	1	91	1	4
H. influenza hem.	4	100	2	3
H. influenza	3	20	5	5
Yeast	2	0	7	7
B. proteus	6	0	1	1
R. Friedlander	2	0	0	0
Pneumococci				

Patients received 60 mg. quills per day (70 mg. quills for four doses for 15 days prior to operation and for two days after operation).

and there were no postoperative pulmonary complications. Because the mucronized forms of the drugs were used in the spring and summer months, a similar but untreated series of cases was analyzed from the summer of 1946, and the incidence of complications was 20 per cent. It should be strongly emphasized that the percentage incidence of postoperative complications does not reflect the severity of the complication. Many were mild and did not prolong the postoperative convalescence appreciably while others were a definite postoperative setback or catastrophe. The true situation cannot be analyzed until more extensive morbidity and mortality data are available. It is obvious that postoperative pulmonary complications in larger series will not be reduced to zero by using mucronized streptomycin as they were in this small series of only forty patients.

The apparent value of the therapy is illustrated by the following case report.

#### CASE REPORT

Case 1 (Strong Memorial Hospital No. 55701)—E. W. J., 60, an old but slender man, admitted to Strong Memorial Hospital on Nov. 11, 1946.

*Presenting Illness*—The patient had a 4-month history of fullness in the epigastrium and regurgitation after eating solid foods, which had become progressively more worse. At the time of admission, he was capable of retaining liquids only and had sustained marked weight loss.

*Physical Examination*—A fairly well developed, somewhat emaciated, 60-year-old man. He appeared bronchial, coughed frequently. The trachea deviated to the left. The chest was hyperinflated with coarse rales audible on the main portion of the bronchial tree. Heart sound over faint and regular. There is moderate right parasternal tenderness and epigastrium, no masses palpable. Remainder of the examination was not remarkable.

*Laboratory*—Examination revealed Weyersmann, negative; red blood cells, 4.65 million; hemoglobin, 17 mg. per cent; hit blood H<sub>2</sub>, 4,000; differential, normal; urine negative; stool, guaiac negative; total protein, 5.6 Gm. per cent; albumin globulin, 3.1/2.5; serum protein nitrogen, 3.5 mg. per cent; alkaline phosphatase, 3.3 Bodsky units. X-ray studies and esophageal gonioscopy established the diagnosis of carcinoma of the distal third of the esophagus.

At the time of admission the patient's general physical condition could not permit surgical removal of the esophageal lesion because of persistent bronchitis, emphysema, and poor nutrition. If operation could be sustained (1) Friedlander bacilli, penicillin resistant; (2) nonhemolytic sulfonamide penicillin sensitive (3, 4 and 5) pneumococci, hemolytic streptococci, and staphylococci all grew in culture. Arterial pneumostomy was started, 2,000 units eight times daily on November 1. After several days of second penicillin therapy the patient was markedly decreased in weight and penicillin-resistant organisms were present, but Friedlander bacilli were not. A transthoracic esophageal resection and esophagojejunostomy were performed on December 5 by one of us (E. H. M.).

On the first postoperative day the patient was alert and conscious but was unable to move dyspneic. There were moist rales over both lung fields and bronchography, as performed by removal of large formal plug of mucus from the right main bronchus, which was cultured. Arterial penicillin started again, an streptomycin was not usable. Bronchography was repeated on the second postoperative day with removal of another mucus plug. Cultures of the aspirated material showed Friedlander bacilli only on both occasions. Course most difficult was throughout both lung fields. Radiocardiogram showed early bilateral congestive pulmonary edema and atelectasis on the left. Streptomycin was started 5 Gm. every 24 hours intramuscularly and 100 mg. every six hours in 1 c.c. saline solution by arterial. On the third postoperative day the patient's lungs were fairly clear and vital signs were definitely improved. Sputum culture on the fourth day after 4 days of streptomycin and arterial therapy revealed no organisms and lungs were clear. He continued to respond rapidly and was discharged on the fifteenth postoperative day.

the fact that it was 100 per cent sensitive to streptomycin preoperatively. It appears that resistance to streptomycin developed rapidly as only 30 per cent of the positive postoperative cultures were streptomycin-sensitive. *V. celer* was also 100 per cent sensitive in preoperative cultures and only one positive culture was found after treatment. It is interesting that in ten out of the forty patients (25 per cent) the postoperative sputum and/or nasopharyngeal cultures were sterile following therapy with streptomycin.

The results of the prophylactic pre- and postoperative use of penicillin and streptomycin by inhalation are summarized in Table V. During the period of time in which this study was in progress, it was impossible to obtain a series of cases in which alternate patients were used as controls, but an attempt has been made to compare the treated patients with similar untreated series. Fifty consecutive major abdominal and thoracic surgical cases were analyzed covering a period of February and March, 1946. Many of the patients in this series of fifty and in the ninety-six control cases studied in 1946 to 1947 received penicillin intramuscularly postoperatively but none received it by inhalation. The patients in all of the control cases were treated with the commonly accepted methods designed to prevent postoperative complications as outlined previously. The postoperative pulmonary complications were divided into three types: pneumonia, bronchopneumonia, and definite atelectasis with or without pneumonia. The patients were followed very closely and with any suspicion of pulmonary complications repeated x-rays were taken.

The gross percentage of pulmonary complications in the periods studied in 1946 to 1947 was 18.0 and 18.7 per cent respectively when no inhalation antibiotic therapy was given. The forty patients receiving penicillin by the atomized aerosol method had 20 per cent incidence of complications, but those receiving the micropulverized form had only a 5 per cent incidence. This difference in results may be due in part to poorer pulmonary penetration of the atomized penicillin. Three patients treated with aerosol developed postoperative pulmonary infections due to penicillin-resistant organisms and these cannot be considered aerosol failures. Forty patients received micropulverized streptomycin

TABLE V. POSTOPERATIVE PULMONARY COMPLICATION

NUM PAT. YES	DATE	TREATMENT	TREATMENT PRE & POST OPERATIVE	PULMONARY COMPLICATION			TOTAL	PER CENT YES
				BRONCHITIS	BRONCHOPNEUMONIA	ATELECTASIS		
56	Feb. & M.	None		4	3		7	
1946								
50	June & July	None		1	7		10	20
1946								
36	Nov. 1946	None		7	11	3	19	19.7
	Apr. 1947							
40	Mar. & Apr.	Aerosol penicillin		0	9	0	9	20
1947								
75	May & June	47 micropulverized		1	0	1	2	2.6
	Nov. & Dec.	47 penicillin						
40	M. & June	Micropulverized streptomycin		0	0	0	0	0
1947								

Dose: Penicillin, 20,000 units four times per d. for two before and after operation  
streptomycin, 100 mg. units three times per d. or q. before and after operation

and there were no postoperative pulmonary complications. Because the micronized forms of the drugs were used in the spring and summer months, a similar but untreated series of cases was analyzed from the summer of 1946 and the incidence of complications was 90 per cent. It should be strongly emphasized that the percentage incidence of postoperative complications does not reflect the severity of the complication. Many were mild and did not prolong the postoperative convalescence appreciably while others were a definite postoperative setback or catastrophe. The true situation cannot be analyzed until more extensive morbidity and mortality data are available. It is obvious that postoperative pulmonary complication in larger series will not be reduced to zero for young micronized streptomycin as they were in this small series of only five patients.

The apparent value of the therapy is illustrated by the following case report.

### CASE REPORT

U S A 1 Strong Memorial Hospital - N 3300J - E W as admitted to Strong Memorial Hospital on Nov 11 1940

**Present illness.**—The patient had no month history of fullness, the epigastric and regurgitation after eating solid foods, which had become progressively more severe. At the time of admission, he was capable of retaining liquids only and had not gained weight eight lbs.

**Physical Exam notes:** A fair well developed somewhat emaciated, 40-year old man who appeared chronically ill coughed frequently. The trachea deviated to the left. The chest was supple without wheezes or crackles over the main portion of the bronchial tree. Heart sound was faint and rapid. There were moderate right egophony tenderness and spaces, no masses palpable. Menstruation of the examination as not remarkable.

Later (ary) - Examination revealed 11 neutrophils, argentophilic blood cells, 467 millions hemoglobin, 17 mg per cc, white blood cell 1000 differential, normal uric acid, normal blood, gastric argentophilic total protein, 3.0 Gm. per cent; albumin globulin, 3.1/3.0 on protein, 24 mg per cent alkaline phosphatase, 3.2 reduced serum Tm. serum at enough given per cent blood be diagnosis of anemia if the ductal th. of the esophagus.

At the time of admission the patient's general physical condition could not permit surgical removal of the myeloma. In view of the patient's leukocytosis, anemia, and poor nutrition the sputum culture results and (1) Friedlander broth, penicillin resistant; (2) methanol; (3) indanazole penicillin resistant; (4 and 5) penicillin sensitive streptococci and *St. ruber*, all from the same source. Second penicillin was started, 3,000 as is right now daily on November 1. After several days of second penicillin therapy the sputum was markedly decreased. Other sputum penicillin and the other tests are almost but Friedlander but the rest and a transference myelogram, myelogram and myelogram-antitoxins are performed on December 3 by our friends (E. R. M.).

On the first postoperative day the patient was alert and cooperative but was unable to move dyspnoea. There are several lines over both lung fields and bronchography performed with removal of large foreign plug of mucus from the right air bronchus. Back as evidenced. Aerial pneumonia started again, an atelectasis a wet rail like bronchography reported on the second postoperative day. A removal of another mucus plug (obstruction of the partial anterior-bowed bronchus) handled only on both air bronchus. Some chest films are like 1 to 1000000 both lung fields. Bronchography is heard early. Additional bronchopneumonia and 1 to 1000000 on the left. Hemothorax is started. 3 lines every 4 hours intravenous alert and 100 mg. cryoexposure is 1 to 1000000 relation by aerial. On the third postoperative day the patient lungs are fairly clear and vital signs are definitely improved. Hemothorax on the fourth day for 10 days of atelectasis via aerial therapy resulted in no signs on and lungs are like 10 continued to upon repeat and 1 to 1000000 on the fifth postoperative day.

We feel sure that if this patient had received both penicillin and streptomycin preoperatively the *in situ* tree could have been sterilized and the postoperative pneumonia prevented. When this patient was studied preoperatively streptomycin was not available in the hospital for prophylactic use. This case demonstrates the clinical value of thorough pre- and postoperative bacterial study of the sputum.

#### DISCUSSION

The results obtained indicate that more emphasis should be placed upon the importance of the normal flora of the respiratory tract in the etiology of postoperative pulmonary infections. The majority of bacteria commonly found in the upper respiratory tract are sensitive to penicillin and/or streptomycin and by using preoperative prophylactic chemotherapy their numbers may be reduced or completely eliminated. Chemotherapy should also be continued for several days after operation until the patient is again able to clear the tracheobronchial tree of secretions, or longer if a specific indication exists. The prophylactic treatment appears to be of specific value if preoperative cultures show bacteria, such as *Streptococcus*, which may be pathogenic. It is particularly important if preoperative cultures show definite pathogens such as *St. hemolyticus*, pneumococci or Friedlander bacilli, as the natural flora of postoperative pneumonias at this time. Bacteria present in the respiratory tract preoperatively. The chemotherapy should obviously be supplemented by all the other prophylactic measures which help to maintain an adequate airway and which clear the bronchi of secretions. The value of postoperative tracheal aspiration with a catheter or with the bronchoscope as a means of preventing or treating atelectasis cannot be overemphasized.

This report indicates a rather high incidence of postoperative complications in the control groups, but the latter influenced by certain factors. Rochester is in an area where an unusually large percentage of the population has chronic sinusitis, and particularly in the winter and spring acute upper respiratory infection are common. The operations included in this series are procedures performed in the upper abdomen and chest which carry a higher incidence of pulmonary complications than lower abdominal procedures or operations out of body cavities. The individuals listed as having bronchitis were not seriously ill from this complication, but were included in the series if they had fever associated with cough and sputum but no pulmonary consolidation. This type usually survives with no specific therapy but they all made extremely unpleasant hospitalizations. The cough, convalescence may be prolonged, and the incidence of abdominal wound disruption is increased. The individuals with bronchopneumonia and/or atelectasis were all seriously ill and in these two groups specific therapy seemed most effective.

It is not the purpose of this report to compare the relative merit of administering penicillin by inhalation in the micronized suspension or in the form of administration by other methods. However, this form appears to have some advantages in surgical patients with pulmonary complication. Specimens of the peripheral portions of the lung have been removed during thoracotomy

after the patient has received the penicillin prophylactically. Appreciable amounts of penicillin are present in the terminal alveoli and there is no microscopic evidence that the contact with the finely powdered penicillin has caused damage to the pulmonary parenchyma. Therapeutic blood levels are obtained by this method and it has been successfully used in the treatment of gonorrheal infections of the genital tract. The reaction of patient to this form of inhalation therapy has been in general, favorable. After preliminary instruction the average adult learns to self-administer the required dose of penicillin and the procedure usually requires less than five minutes. In our experience most patients prefer the method of inhalation to repeated needle punctures and less time is required in the administration of the micropowdered form than with the mist type aerosol method. There are also some disadvantages in this method of administration. Three patients have developed urticaria during treatment and one developed a mild asthmatic attack. Sore throat occasionally develops and is characterized by redness and swelling of the mucous membranes, but it subsides as soon as the therapy has been discontinued and is symptomatically relieved by the oral administration of antihistamine drugs such as Benadryl.

# SUMMARY

The incidence of postoperative pulmonary infections can be greatly reduced by the prophylactic administration of penicillin and streptomycin. The administration of these antibiotics by inhalation in the micropowdered form has been found to be a satisfactory method and relatively small doses of the chemotherapeutic agent are required.

Factors present in the upper respiratory tract preoperatively are important factors in the genesis of postoperative pulmonary infection. Reduction of respiratory complications following upper abdominal and thoracic surgery can be accomplished by measures which minimize atelectasis and promote pulmonary ventilation in conjunction with inhalation chemotherapy.

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# THE SIGNIFICANCE OF HEMOPTYSIS IN CARCINOMA OF THE THYROID GLAND

## HISTORY OF FOUR CASES

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MALIGNANCY arising in the thyroid gland has long been an interesting problem, especially in regard to its incidence and treatment. The frequency of malignant disease of the thyroid gland is difficult to determine. Various reports in the literature indicate the incidence to be from 1.6 to 4.8 per cent. Nevertheless, the possibility of the presence of malignancy in a given case is so infrequently estimated that many times a hopeless state has been reached before definitive treatment is instituted.

The early signs and symptoms of carcinoma of the thyroid gland are few and certain none are pathognomonic. Most carcinoma occurs in nodular goiters, and an increase in the rate of growth of such a gland should make one suspect the presence of a malignant change. Once the invasive process has escaped the confines of the gland some degree of fixation develops, usually in the region of the trachea. If the process is allowed to proceed unchecked actual malignant invasion of the trachea, esophagus, larynx, or hypopharynx may occur. Cough at first productive later blood stained, is likely to develop. On the other hand, repeated small or large hemoptyses may occur without an accompanying cough.

The presence of hemoptysis, whether or not a visible or palpable goiter is present, should suggest the possibility that malignant invasion of the trachea, larynx, esophagus, or hypopharynx has occurred. In four patients seen at the University of California Hospital hemoptysis was prominent symptom drawing attention to the possibility of malignant change in a goiter of long duration.

## CASE REPORTS

CASE I. A 65 year old man, entered the University of California Hospital Sept. 13, 1937, stating that for several years he had noted bleeding from the mouth and throat, which occurred usually spitting but on occasion a heavier flow. Several hemorrhages, twice of about 50 cc. occurred shortly before entry. A goiter present for at least twenty years, but enlarging for ten years, and in the six months prior to entry the patient had lost 15 lb. in weight. He had no pain, pressure or obstructive symptoms, nor did he notice changes in his voice but he was a little hoarse feeling in the throat.

An irregular enlargement in the region of the thyroid gland displaced the trachea to the right. The lower third was more prominent on the left side and extended freely upon motion and was about a cent. above the deep structures. No bruit or thrill apparent. There were several palpable lymph nodes in the right and left supraclavicular fossae. Indirect laryngoscopy showed normal structures throughout.

At operation an inflammatory mass occupied the upper third of the left lobe. A third, fourth and fifth tracheal rings displaced the trachea, occupied the entire width, and could not be detached from the anterior surface of the trachea. This mass was removed as completely

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possible long in both thyroid lobes the tumor lay in contact with the trachea (Fig 1). Microscopic examination revealed papillary carcinoma of the thyroid gland.

The patient received radiation therapy postoperatively in right and left lateral neck fields (1,660 r). He died eight months after removal of carcinoma of larynx.



Anterior surface view of  
tumor on anterior trachea

Fig 1 (Case 1).—The trachea displaced the right lobe of the thyroid gland, as left lobe is displaced by carcinoma. Destruction of the cartilaginous rings has occurred, thereby producing deformity. Complete surgical removal of the tumor impossible.

Case 2.—M. H. H., 23-year-old male, born in California, Hospital No. 4, 1940, complaining of almost constant dyspnea worsened by exertion, by hacking cough, and increase in hardness of gradually hoarse voice for the previous six weeks. The patient stated that in 1933, at the age of 15 years, he had noted firm, slow-growing mass in the right anterior part of the neck which caused no symptoms. He received Lugol solution for six months without noticeable effect. The nodule was removed surgically elsewhere in 1936. Ten years later the nodule reappeared, growing progressively larger. Its former size but remaining asymptomatic. In 1939, right lobectomy performed elsewhere. The thyroid gland was said to be very lobulated. The nodule grew and slowly increased in size until the patient's entry in 1940.

The patient underwent the third partial right lobectomy, Sept. 5, 1940. The nodule had broken through the deep and superficial fascial layers in the midline on the trachea so that they had split down to the skin and subcutaneous tissue in the suprasternal notch. The left lobe appeared normal and the entire normal. The right side of the neck completely filled with large mass of multiple nodules which are very soft and cellular. The tumor mass extended well down to the right chest and well back behind the trachea on the right. There had been some erosion of the trachea just below the thyroid cartilage. The entire right-sided mass was removed as far as the thyroid tissue remained, far as could be determined (Fig 2). (Histologic diagnosis of papillary thyroid adenoma and degenerating adenoma. No metastatic carcinoma.)

This patient reentered the University of California Hospital, Nov. 24, 1946, stating that for as long as year previously he had had minor hemoptysis, which were said to be due to metastatic cancer on the posterior trachea. Two months before entry he had noted

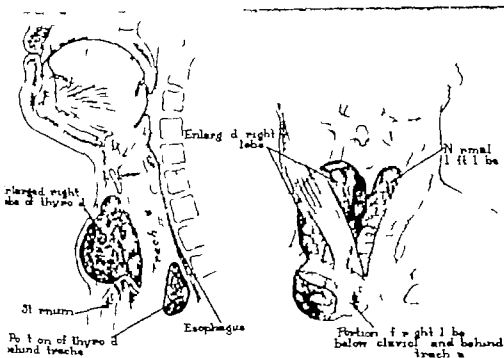


FIG. 2 (Case 2).—The left side of the neck is filled with masses of multiple adenoma which had broken through the deep and superficial fascia but no erosion of the cartilages was noted at this time. The right-sided mass removed postoperatively.

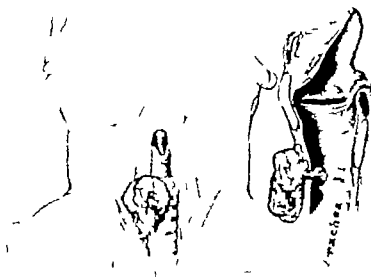


FIG. 3 (Case 3).—The recurrent laryngeal nerve is limited to the right side. C indicates the area where the nerve was destroyed. The trachea is shown in the center. The trachea is shown in the center. The trachea is shown in the center.

recurrence of the nodules over the trachea which grew slowly but progressively in size. One week previously she had had hemoptysis of bright red blood (about 200 cc) without systemic symptoms. Pharyngeal, laryngeal, and bronchoscopic examinations failed to reveal the site of the hemorrhage. A roentgenogram of the chest showed no abnormal findings.

Reevaluation of the material removed at operation in 1940 revealed several vascular channels showing invasion of their lumina by neoplastic tissue. Hence the diagnosis was histologic demonstration of the thyroid gland.

At surgery Nov. 29, 1944, there was no thyroid tumor in the usual location of the right lobe. Lying along the cricoid cartilage and just below it was a mass of tissue about 4 cm. in diameter which had eroded through the cartilaginous rings on the posterolateral surface so that there was an absence of cartilage for distance of least 3 mm. At this level mass of tissue measuring about 5 mm. in diameter projected into the trachea (Fig. 3). This was removed together with the tumor in the anterior neck. It was then possible to close the trachea

adenocarcinoma (recurrent)  
ery there has been no recur

recurrence of the tumor nor of the hemoptysis

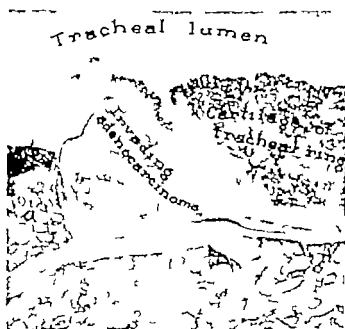


Fig. 4 (Case 3).—Photomicrograph of a portion of the invaded trachea. Invasion of the cartilaginous tracheal rings is evident. The macroscopic pattern is one of an adenocarcinoma.

CASE 3.—P. F., 66-year-old American Italian woman, came to the University of California Hospital in November, 1944, stating that for two months she had experienced hemoptysis and regurgitation of mucous-gangrenous material, plus in the anterior cervical region and choking sensation when swallowing. She had lost considerable weight in the previous 6 months. At about this same time she

occupying the right thyroid lobe. Fixation of the deep tissues was evident, and the trachea was moved with the following. The trachea was deviated to the left. Indirect laryngoscopy revealed a large (3 by 1.5 cm.)

mouth, spongy mass in the region of the isthmus and pharyngeal all having the appearance of its lobes separated by shallow notches of iron. There was evidence of recent bleeding from the superior aspect of the right side of the mass (Fig. 5).

Very close of the best (sagittal) normal view of the neck showed partially calcified mass on the right side in the region of the thyroid gland. The trachea and the esophagus are displaced to the left and considerable displacement of the esophagus to the level of the larynx immediately anterior to the fifth and sixth cervical vertebrae was apparent. The trachea was only slightly compressed when the lateral view (Fig. 6).

Rough Sketch

Tissue displacing esophagus and trachea

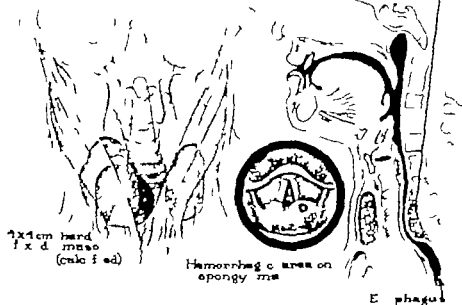


Fig. 5 (C = 3).—The partially calcified mass displaces the trachea to the left and is firmly adherent to it and the larynx. Extension has occurred into the hypopharynx presenting as a lobulated tumor partially covering the vocal cords. The hemorrhagic area indicates the source of the hemorrhage. The esophagus is displaced forward by malignant tissue lying posterior to it.

The first biopsy from the hypopharyngeal mass showed only submucosal hemorrhage with organization. However, second biopsy (in effect partial removal of the tumor) showed the hypopharyngeal tumor to be papillary adenocarcinoma of the thyroid gland.

During December 1934 the patient was given roentgen therapy (6,000 through right and left lateral neck field). Such resulted in considerable decrease in size of hypopharyngeal tumor. On examination three weeks and fifteen months after the completion of therapy the larynx and vocal cords or entire normal in appearance, and there was no evidence of metastases other than the hard. The mass in the right thyroid lobe by this time had become even more fixed and hard. Roentgenograms of the neck showed the anterior displacement of the esophagus to be essentially the same as in 1934.

Since the hypopharyngeal tumor had disappeared by radiation therapy there were hopes that the primary tumor might be eradicated. Hence the patient was operated upon in October 1934. A rocklike tumor of granular consistency found to be adherent to the stomach wall, esophagus and was fixed adherent to the larynx and trachea.

recurrence of the tumor in the trachea which grew slowly but progressively in size. One week previously she had had hemoptysis of bright red blood (about 200 cc) without systemic symptoms. Pharyngeal, laryngeal, and bronchoscopic examinations failed to reveal the site of the hemorrhage. A roentgenogram of the chest showed no abnormal findings.

Re-examination of the material removed at operation in 1940 revealed several vascular channels showing invasion of their lumina by neoplastic tissue. Hence the diagnosis was benign but invasive carcinoma of the thyroid gland.

At surgery Nov. 29, 1946, there was no growth of tumor in the usual location of the right lobe. Lying along the cricoid cartilage and just below it was a mass of tumor about 4 cm in diameter which had eroded through the cartilaginous ring on the posterolateral surface so that there was an breach of cartilage for a distance of about 3 mm. At this level mass of tumor measuring about 5 mm. in diameter projected into the trachea (Fig. 3). This as removed together with the tissue in the anterior neck. It was then possible to close the trachea with ureteral catgut and reinforce the ring with 000 catgut sutures.

Histologic examination showed the excised tumor to be an adenocarcinoma (recurrent) of the thyroid gland (Fig. 4). In the fourteen months since surgery there has been no recurrence of the tumor nor of the hemoptysis.

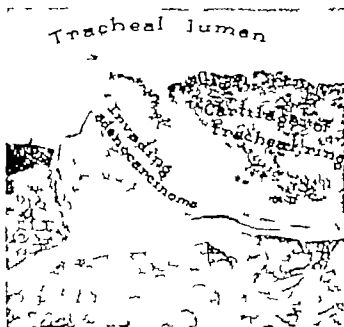


Fig. 4 (Case 3).—Photomicrograph of portion of the invaded trachea. The union and destruction of the cartilaginous tracheal ring are evident. The microscopic pattern is one of an adenocarcinoma.

CASE 3.—F. P., 50-year-old American Indian woman, came to the University of California Hospital in November 1944 stating that for months she had experienced recurrent hemorrhages of mucousanguineous material, pain in the lower cervical

lobes. Presection of the deep tissues was excised and the tumor in the trachea was removed. The left thyroid laryngoscopy revealed large (3.0 by 1.5 cm)

smooth, spicary mass in the region of the right subglottic lymph node. The upper part of the lobes separated by shallow recesses from the trachea. There was no evidence of recent bleeding from the superior part of the right side of the mass (Fig 5).

Very close to the best possible normal view of the neck showed partially calcified mass on the right side in the region of the thyroid gland. The trachea and the esophagus were displaced to the left and considerable displacement of the esophagus at the level of the larynx. The trachea was displaced forward and the fifth and sixth cervical vertebrae were prominent. The trachea was slightly compressed when the larynx was viewed (Fig 6).

Figure 5

Tissue displacing esophagus and trachea

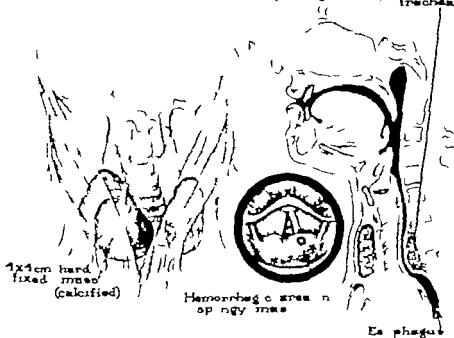


FIG. 5. Case 2.—The partially calcified mass displaced the trachea to the left and is firmly adherent to it and the larynx. Extension has occurred into the hypopharynx presenting as a lobulated mass partially covering the vocal cords. The hemorrhagic area indicates the source of the hemoptysis. The esophagus is displaced forward by anterior displacement of the trachea.

The first biopsy from the hypopharyngeal mass showed only subacute hemorrhage and organization. However, second biopsy (in effect partial removal of the tumor) showed the hypopharyngeal tumor to be papillary carcinoma of the thyroid gland.

During December 1944 the patient was given roentgen therapy (6,000 through right and left lateral neck field) which resulted in considerable decrease in size of hypopharyngeal tumor. On examination three, twelve, and eighteen months after the completion of therapy the larynx and vocal cords were all well normal in appearance, and there was no evidence of metastases within the field. The mass in the right thyroid lobe by this time had become even more fixed and hard. Roentgenograms of the neck showed the anterior displacement of the esophagus to be essentially the same as in 1944.

Since the hypopharyngeal tumor had disappeared by irradiation therapy there was some hope that the primary tumor might be eradicated. Hence this patient was operated upon in October 1945. A rocklike mass of granular consistency, fixed to the surrounding tissue, was removed and the esophagus and was firmly adherent to the larynx and trachea.



Puckering on the mucosal surface of the esophagus could be felt through the patient's mouth. The tumor seemed complete and could be done without ends giving the larynx an esophagegus.

Radiation volume (236 m rads) was given preoperatively in the hope that the tumor would take up the radiation in a quantity sufficient for treatment. However none of the radiolabel material was absorbed by the tumor.



FIG. 4 (Case 2).—Photograph of roentgenogram showing the anterior displacement of the esophagus by the level of the larynx by invasion of malignant tissue posterior to it.

The patient was discharged for follow-up care to her own County Hospital after she declined further radiation therapy at this hospital. She lived less than a month after surgery. At this time there was evidence of tracheobronch metastases and of local recurrence. Weight being almost equal.

CASE 4.—R. P., 60 yrs. old white male, came to the University of California Hospital stating that he had noted progressive symptoms of hoarseness, difficulty in clearing the throat and dysphagia for the preceding ten years. Six months prior to admission he noted firm, painless swellings in the lower anterior part of the neck. It had gradually increased in size. There had been an occasional small hemoptysis.

Physical examination revealed an elderly man showing evidence of chronic debilitating disease. A dry hacking cough with hoarseness and hoarse cough were noted. A mass in the lower anterior cervical region, apparently an enlarged thyroid gland displaced the trachea to the right and was firmly adherent to the trachea and the surrounding structures. There were no palpable lymph nodes.

Indirect laryngoscopy revealed swelling and anterior fixation of the arytenoids. The false cords were level for phonation. The larynx was compressed so that the anteroposterior diameter was lowered. The cord on the left was situated at a somewhat swollen, but still not evident mucosal erosion (Fig. 5). X-rays revealed no air in the larynx.

The mass in the thyroid gland together with the nodal or nodal enlargement posterior to the trachea and the presence of primary thyroid metastases involving through the thyroid cartilage into the larynx. However, biopsy of the anterior cervical mass showed it to be composed of squamous cell carcinoma, pointing distally toward primary focus in the larynx.

Because of the possibility that metastatic lesions were of the cartilaginous type and that the larynx had already occurred, surgery appeared advisable. A total laryngectomy with sub-

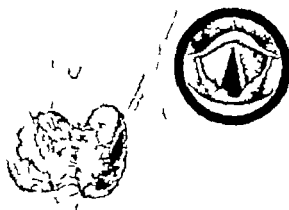


FIG. 7 (Case 4).—The larger left thyroid lobe displaces the trachea slightly to the right. The gland is firmly adherent to the deep structures, especially the larynx. The trachea, seen in the left and right in an unobstructed position, which has invaded the larynx and the left lobe of the thyroid gland.



FIG. 8 (Case 4).—[Photomicrograph illustrating the characteristic] areas of carcinoma of the thyroid gland, which have invaded the thyroid gland.

total resection of the involved thyroid gland was done. The right lobe of the thyroid gland was normal and exhibited discrete capsule. The left lobe which was firm and nodular adherent to the sternothyroid muscle and to the trachea and thyroid cartilage. This portion of the thyroid gland along with the adherent sternothyroid muscle was removed with the larynx.

Study of the specimen showed that the primary tumor had arisen in the left vocal cord. There was union by squamous cell carcinoma of the left thyroid cartilage, left lobe of the thyroid gland, left sternothyroid muscle and the sternocleidomastoid muscle of the neck (Fig. 8). In the fourteen months following surgery the patient gained fifteen pounds and developed an esophageal mass. There was no evidence of recurrence of the malignant process.

#### DISCUSSION

Direct extension of malignant disease of the thyroid gland into adjacent structures account for fixation and for the possible occurrence of hemoptysis. The closely packed nature of the structures of the neck makes for malignant involvement of the trachea, larynx, esophagus, or hypopharynx at a rather early stage in the progress of the disease. Hemoptysis may be the only symptom of which the patient complains; he may be entirely unaware of a goiter. The possibility of a secondary malignancy from a primary lesion in the thyroid gland should not be overlooked. Hemoptysis may also occur with a lesion primary in the larynx, trachea, or hypopharynx secondarily invading the soft structures of the anterior compartment of the neck, notably the thyroid gland.

In some instances, laryngoscopy or bronchoscopy may fail to reveal intra-tracheal malignant invasion if the lesion is well hidden by intact vocal cord. In most cases, however, the presence or absence of malignant involvement can be determined by such procedures. Usually the process assumes a polypoid form if it projects freely into the tracheal or laryngeal lumen. When the hypopharynx is involved, a bulging mass overlapping the vocal cord may be seen. Mucosal ulceration may not be demonstrable in spite of a definite history of hemoptysis.

The real flag of hemoptysis unfortunately is a danger signal received too late. When the carcinoma has grown through its capsule and has infiltrated the surrounding tissue and invaded other structures of the neck, it has reached an incurable state. The early discovery of firmness, fixation and evidence of invasion in a goiter showing accelerated growth immeasurably adds to the possibility of cure of carcinoma of the thyroid gland. Efforts should be directed toward establishing the diagnosis and instituting treatment at the earliest possible moment.

#### SUMMARY

Four patients complaining primarily of hemoptysis in the presence of a goiter noted for varying periods of time were found to have malignant disease in the thyroid gland. In three cases the primary disease was carcinoma of the thyroid gland; in the fourth a squamous-cell carcinoma of the vocal cord had secondarily invaded the thyroid gland. These cases are reported in an effort to emphasize the fact that hemoptysis in association with goiter, especially one which has shown recent growth, should indicate malignancy of the thyroid gland, or a malignancy primary in the larynx or hypopharynx secondarily invading the thyroid gland.

# CLINICAL AND LABORATORY STUDIES ON THE UPTAKE OF RADIOACTIVE PHOSPHORUS BY LESIONS OF THE BREAST

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TISSUES in which there is markedly increased metabolic activity such as acute inflammation and rapidly growing tumors show increased concentration of phosphorus when compared with similar normal structures. A study of the uptake and concentration of tracer doses of radioactive phosphorus by various pathologic conditions of the female breast was begun at the University of California Hospital in October 1954.

Eighty patients with various types of breast lesions have been given tracer doses consisting of 300 to 500 millicuries of radioactivated phosphorus ( $^{32}\text{P}$ ) as disodium-hydrogen phosphate ( $\text{Na}_2\text{HPO}_4$ ) solution intravenously. Radioactivity over body surfaces was detected with a Geiger Mueller counter with a counter tube having a circular window 2 cm in diameter placed at a distance 18 mm from the body surface. Skin surface measurements of radioactivity were made in 100 patients over breast lesions and over comparable areas in the opposite normal breast over enlarged axillary and cervical gland and comparable areas on the opposite side and over superficial nodules in the breast areas in which the possibility of metastatic malignant disease or inflammatory processes were suspected. Usually several series of measurement were made during a period of forty-eight hours following the administration of the tracer dose of radioactive phosphorus. In the patients who required operation for breast lesions the tracer dose of radioactive phosphorus was given forty-eight hours prior to operation. Weighed parts of the breast lesions and of contiguous comparable normal tissues removed by operation were reduced to ash and determinations of their radioactivity made by the Geiger Mueller counter. Finally the radiologic, clinical, and pathologic data were correlated.

Complete clinical, radiologic and pathologic data are available on sixty-two of the eighty patients studied by the skin surface measurement method. Figures 1 to 6 are diagrams indicating actual skin surface Geiger Mueller (scale of 8) measurements on some of these patients. Table I demonstrates the method used for recording the data obtained by Geiger Mueller counter from skin surface measurement following the administration of tracer doses of radioactive phosphorus.

Twenty-one patients had benign lesions of the breast. Data on these patients are recorded in Table II.

Forty-one patients with malignant disease of the breast were studied by this method, and data on these cases appear in Table III.

1. Read the writing of the book of Umberto Bergomi New Orleans La. on 23-21

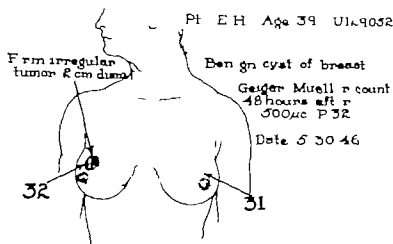


Fig 1—Diagram indicating skin surface radiation measurements (Geiger Mueller counter readings scale of 1) over benign cyst of right in left breast with comparable area over apparently normal opposite breast.

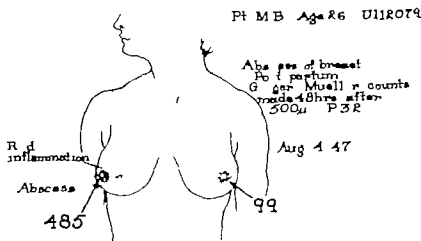


Fig 2—Diagram indicating skin surface radiation measurements (Geiger-Mueller counter readings scale of 5) over acute abscess infection of the right breast.

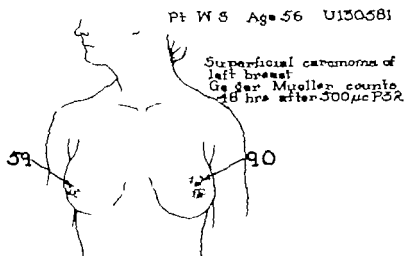
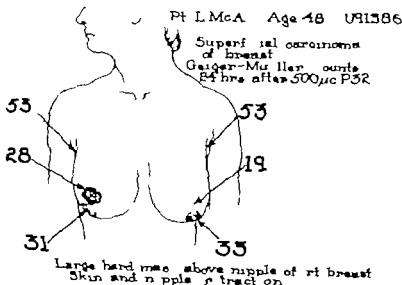


FIG. 1—One of two and two days after treatment measurements (Geiger Mueller counter readings) with Geiger Mueller counter of the left breast compared with opposite apparently normal breast.



Geiger  
counter  
readings  
with  
skin  
and

Geiger counter  
right breast  
also compared  
1 or 2 days

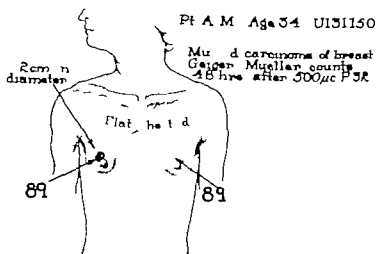


Fig. —Diagram indicating skin surface of the neoplasms (Geiger Mueller counts made of ) over incised carcinoma of right breast prior to (left) and (right) normal left breast.

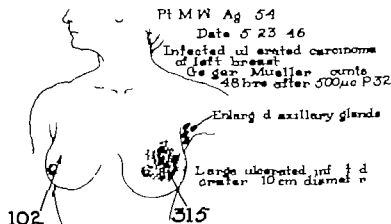


Fig. —Diagram indicating skin surface of the neoplasms (Geiger Mueller counts made of ) over large ulcerated infected carcinoma of the left breast.

Pt R H Age 34 U129253

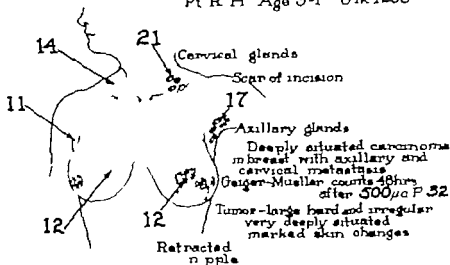


Fig. 1—Diagram indicating skin surface radiation measurements (Geiger-Mueller counts of readings scale of 1) over deep situated (more than 0.5 cm beneath skin surface) carcinoma in very upper left breast. Not identical readings over breast as left breast as compared to normal right breast, and farthest readings over relatively more superficial left breast and left cervical metastasis compared with upper right axilla and neck regions.

Pt J W Age 33

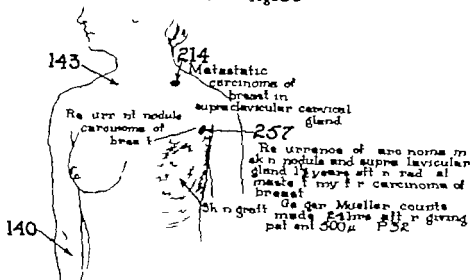


Fig. 2—Diagram indicating skin surface radiation measurements (Geiger-Mueller counts of readings scale of 1) over recurrent carcinoma of the breast.



TABLE I. SAMPLE CALCULATION

		GROUP B FLIP 13 AND 64 (BC OF B)	
		OTOLAL HEALING	FLIPING AT 16 WOUNDS
Background		5 (8)	
Vertical skin surface		30 (9)	25 (9)
Skin surface over breast tumor		50 (8)	45 (8)
Difference	(45-25) (8) = 20 (8)		
	20 (8) = 100%		
	40 (8) = 100% = 100%		
	25		
Most malignant tumor in interstitial breast lesion		5% of more	
Most benign lesions less than 25%			

TABLE II. SKIN SURFACE MEASUREMENTS OF CONCENTRATIONS OF RADIUM-226 IN THE FLIP 13 AND 64

Epidermal disease			
Epidermal tumor	4	4	0
Epidermal papilloma			0
Clinical, benign (not operated)	1	1	0
Total	17	1	1
Interstitial fibrosis with necrosis and necrotic hemorrhage	1	0	1 (116%)
Interstitial fibrosis	1	0	1 (30%)
Healing necrotic marginal necrosis	1	0	1 (15%)
Malignant fibrosis necrotic necrosis	1	0	1 (110%)
Total	1	0	1

Skin surface measurements of concentrations of radium-226 in the flip 13 and 64. The flip 13 and 64 were taken after administration of tracer dose (200 to 500 microcuries) over the skin lesions and interstitial areas of the breast.

Interstitial studies of tumor tissue and normal breast tissue show high phosphorus concentrations in the benign breast lesions.

TABLE III. SKIN SURFACE MEASUREMENTS OF CONCENTRATIONS OF RADIUM-226 IN THE FLIP 13 AND 64

	FLIP 13		FLIP 64	
	PPH OF FLIP	TR OF FLIP	PPH OF FLIP	TR OF FLIP
Epidermal disease	12	0	12 (1)	14 (1)
		0	(A)	100%
	1	1	0	
	2	0	0	
	1	1	0	
	4	0	4 (A)	100%
		1	1	
	4	0	4 (A)	100%
	7	0	7 (A)	100%
			6 (A)	100%
Total	1	1	1	1

Skin surface measurements of concentrations of radium-226 in the flip 13 and 64. The flip 13 and 64 were taken after administration of tracer dose (200 to 500 microcuries) over the skin lesions and interstitial areas of the breast.

## SUMMARY

Skin surface measurements of radioactivity were made on 80 patients with lesions of the breast following the administration of tracer doses of radioactive phosphorus. Clinical radiologic and pathologic data are complete in sixty-two. Sixteen out of seventeen patients with benign breast lesions including fibrocystic disease, fibroepithelial tumors, and papilloma gave skin surface measurements comparable to that of normal skin, forty-eight hours following tracer doses of radioactive phosphorus, and an unexplained increased reading was obtained in one case. In some cases increased readings were obtained over the nipple areas. Measurement made in four patients with benign inflammatory lesions showed markedly increased radioactivity over the inflamed areas.

Radioactive phosphorus uptake studies were carried out in forty-one patients with malignant disease of the breast. Skin surface measurements of radioactivity made over cellular types of primary breast carcinoma, axillary and cervical metastatic lesions, and local recurrent carcinomatous nodules all exceeded by more than 50 per cent measurements taken over comparable apparently normal tissues. Measurement made over ulcerated infected carcinomatous lesions were markedly increased. Measurements taken over very small (microscopic in size) malignant lesions, mucoid carcinoma of the breast, and over lesions deeply situated (more than 0.5 cm. from the skin surface) in obese breasts were comparable to those made over the skin overlying normal breast tissue. In two patients who had had hormone therapy and irradiation for carcinoma of the breast, one showed increased readings over the diseased breast tissues and one did not.

## CONCLUSION

Geiger-Mueller measurements of skin surface radioactivity made over breast lesions during the forty-eight hour period following the administration of tracer doses of radioactive phosphorus (300 to 500 microcuries) give interesting and useful data for the clinical, radiologic and pathologic study of breast lesions. (This method cannot be used at this time for radiation therapy for lesions of the breast.)

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TABLE I SAMPLE CALCULATION

	GROUP M KILLER SPREADSHEET (SCALE OF 8)	
	ACTUAL READING	READING MINUS BACKGROUND
Background	5 ( 8 )	
Normal skin surface	30 ( 8 )	25 ( 8 )
Main surface over live & tumor	50 ( 8 )	45 ( 8 )
Difference	(45-5) ( 8 ) = 20 ( 8 )	
	25 ( 8 ) = 100%	
	20 ( 8 ) = 80%	100% = 40%
	3	
Most malignant adjacent inflammatory breast lesion 55% or more		
Most benign lesion less than 55%		

TABLE II SKIN SURFACE MEASUREMENTS BEARING INDEX OF THE TUMOR

	TIME H	KILLER SPREADSHEET OPT 17	
		ACTUAL READING	READING MINUS BACKGROUND
Benign disease	10	9	1 ( 116% )
Fibroadenoma	4	4	0
Benign papilloma	3	3	0
Clinically benign (not operated)	1	1	0
Totals	17	16	1
Intraductal fibroadenoma with necrosis and recent hemorrhage	1	0	1 ( 116% )
Acute pyogenic infection	1	0	1 ( 116% )
Healing recent surgical incision	1	0	1 ( 116% )
Subcutaneous infection around suture	1	0	1 ( 116% )
Totals			4

\*Adjuvant phosphorus twenty-four  
(24 to 54 micrograms) over 10  
and high phosphorus concentration

TABLE III SKIN SURFACE MEASUREMENTS IN MAIN

	TIME H	KILLER SPREADSHEET OPT 17	
		ACTUAL READING	READING MINUS BACKGROUND
	12	0	12 ( 1 )
	2	0	2 ( 1 )
	3	1	0
	3	3	0
	1	1	0
	4	0	4 ( 1 )
	4	1	1
	4	0	4 ( 1 )
	5	0	5 ( 1 )
		8	8 ( 1 )
Totals	41	21	

\*Skin surface measurements of each fraction of radiophosphorus twenty-four to  
forty-eight hours following administration of tracer dose 24 to 54 micrograms in main  
area of the breast.

Substitution accidents may occur in several ways. The error may have been made in the pharmacy where either the wrong or an improper solution was made or the final package was improperly or incompletely labeled and identified. Of more frequent occurrence in our opinion, is the error made by the nurse, or the house officer or the surgeon himself who having several colorless solutions such as alcohol ether procaine cocaine and saline on the instrument tray may draw into the syringe the wrong solution for injection. This latter mistake seemingly easily avoidable nevertheless, occurs all too often.



Fig. 1—Referred case. Complete sloUGH of the penis following circumcission after injection of supposed local anesthetic. A small projection below the patello symphysis represented the root of the penis, through the center of which urine as voided in "gun-shaped stream."

#### IDENTIFICATION OF PROCAINE

In many large hospitals procaine solution are prepared in bulk either in the pharmacy or in the central supply room. Since this method has certain advantages other than economy it is imperative to be able instantly to distinguish and identify procaine from all other colorless solutions.

Owing to the danger of being misunderstood when procaine is pronounced indistinctly and of the substitution of cocaine great care should be taken when procaine is ordered verbally.

**Odor**—A 1 Gm. pellet of chlorobutanol added to several liters of procaine solution will not only act as a preservative but will impart a faint odor. Because

## THE PREVENTION OF CHEMICAL BLOUHS

IDENTIFICATION OF PROCAINE, ALCOHOL, ETHER, BORIC ACID, AND OTHER COLORLESS SOLUTIONS COMMONLY USED IN THE OPERATING ROOM

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THE usefulness of the procedure of local anesthesia as practiced by many surgeons, as a substitute for general narcotics for operations of short duration is universally admitted. The injection of an anesthetic solution at random in the structures to be cut through requires little skill or experience and can be performed almost indiscriminately in all parts of the body. Despite the simplicity of the procedure accidents from the administration of local anesthetics have undoubtedly been more numerous than one would be led to believe from the few isolated cases which have been reported. While this may be construed as indicative of the infrequency of such accidents, it is probable that many cases will not reach the literature. If the latter should be true we may be lulled into a false sense of security. We believe that more accidents and reactions occur as the result of injection of the wrong solution than those due to sensitivity to the anesthetic agent. Few surgeons experiencing the misfortune of administering the wrong solution have recorded the accident though a service might have been rendered by repeatedly calling to the attention of the medical profession the possibility of mistakes, and emphasizing the need for utilizing the known safeguards in an effort to prevent them. Furthermore discussion may stimulate investigation which may lead to better prophylaxis. It is with this idea in mind that we submit the present study.

Reactions from local anesthetic agents may be divided into three types: (1) those presumably dependent upon true hypersensitivity of the patient to the drug, (2) those resulting from the absorption of a toxic dose of the drug, and (3) those resulting from the administration of the wrong solution. It is with the third aspect of the problem that we are primarily concerned here.

Solutions which may be mistaken for procaine can be divided into three classes, the common factor being that they are colorless, and are used frequently not only in the operating room but throughout the hospital. Class I necrotizing solutions such as alcohol, the boric acid, concentrated glucose phenol, and formalin. The injection of these material will induce anesthesia, but necrosis of tissue will ensue (Figs. 1 and 3, A and 4, A). Class II biologically potent preparations, such as adrenalin hydrochloride, cocaine hydrochloride, atropine sulfate, morphine sulfate, etc. These solutions may cause death if administered in sufficient quantity. Class III less potent solutions, such as distilled water, hydrogen peroxide, sodium lactate, etc. may cause severe reactions. (Figs. 2, 3, B and 4, B).

This work was aided by grant to Duke University by the W. M. Beck Inc. Foundation. N. Y. Read at the meeting of the Society of Plastic Surgeons, New Orleans, La., Jan. 28-4, 1949.

of the presence of the oil  $\text{m}$ , which may mask that of the chlorobutanol this method of identification is not reliable.

*As for Tests*—The surface tension of an aqueous solution is such that procaine tends to cling to syringe plunger whereas alcohol does not stay in droplets but flows out rapidly over the gloved hand. Ether likewise tends to disperse and evaporates rapidly. While this method may be helpful the reaction may not always be distinct especially when the gloves are wet.

*Colored Bottles*—Even though procaine or other colorless solutions are packaged in different colored bottles, they immediately lose their identity when poured out of the original container to be made ready for use. Although the possibility of error may be lessened when the solution is drawn from a rubber stoppered container  $\text{m}$ , likewise, stock solutions which are used for numerous injections are seldom suitable and their routine use is not encouraged.

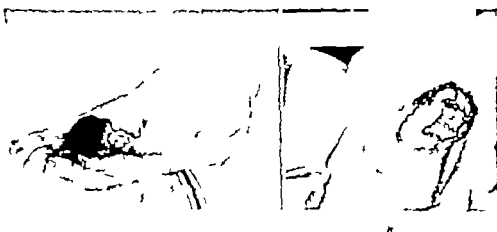


FIG. 4.—Left: (a) development of lesion developing after injection of alcohol instead of local anesthetic for removal of skin. Right: (b) development of lesion after injection of distilled water.

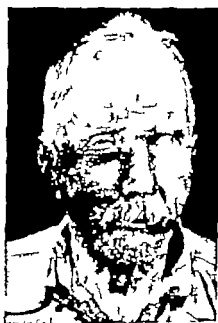
*Colored Bottles and Vials*—For some years brilliantly colored porcelain beads were added to small flasks and containers to identify the solution. Large colored marbles or glass spheres were put in large flask and the identifying bead or marble would accompany the solution when it was poured out of its original container. This method of identification was a very satisfactory one. However, the use of beads and marbles ceased, and domestic manufacturers' resources were curtailed, so that these objects were no longer available.

*Test of the Solution*—Since the procaine solution itself can be tinted a characteristic color this method has the advantage over all other methods in that the solution is identified in the syringe before injection.

Procaine is the diethylaminoethyl ester of  $p$ -aminobenzoic acid related to the sulfonamide compounds and so gives many of the chemical reactions of these compounds. When methylmagnesium iodide, benzaldehyde, added



A



B

Fig 2--Referred cases. A. An infant given fluids and the area of the scalp. When the dressing was removed several days later it was found that large ulcers had developed. B. A lesion developed over the scalp region of this elderly man. An unknown preparation was injected. Forty-eight hours later an extensive hemorrhagic ulcer had developed.



A



B

Figure 3--Indication of the upper lip. The other side was removed by excision and the lip previously split. An incision on right breast. See the section of section tissue which had not been

of the presence of ether clouds, which may mask that of the chlorobutanol this method of identification is not reliable.

**Surface Tension.**—The surface tension of an aqueous solution is such that procaine tends to cling to surgical gloves in beads whereas alcohol does not stay in droplets, but flows out rapidly over the gloved hand. Ether likewise tends to impave and evaporates rapidly. While this method may be helpful the reaction may not always be distinct especially when the gloves are wet.

**Colored Bottles.**—Even though procaine or other colorless solutions are packaged in different colored bottles, they immediately lose their identity when poured out of the original container to be made ready for use. Although the possibility of error may be lessened when the solution is drawn from a rubber stoppered container nevertheless, stock solutions which are used for numerous injections are seldom reliable and their routine use is not encouraged.



FIG. 1.—Fig. 1. A. Procaine on surface after injection of alcohol instead of local anesthetic or immersion of tooth.

B. Alcohol following solvent action administration of distilled water.

**Colored Beads and Marbles.**—For some very rare, brilliantly colored porcelain beads were distributed in all flask and containers to identify the solution. Large colored marbles, glass spheres were put into large flasks, and the identifying beads or marbles would accompany the solution when it was poured out of its original container. This method of identification was a very satisfactory one. During the war however important materials, beads and marbles ceased, and domestic manufacturers' resources were curtailed so that these objects were, and still are somewhat difficult to obtain.

**Tint of the Solution.**—Since the procaine solution itself can be tinted a characteristic color this method has the advantage over all the methods in that the solution is easily identified in the vial before injection.

Procaine, the diethylammonium salt of para-aminobenzoic acid, is related to the sulfonamide group and also to the group of the chemical reactions of these compounds. When *n*-butyl, 3-methyl-4-hydroxybenzaldehyde is added



to a solution of procaine, a golden yellow color is formed. The reaction depends upon the formation of a colored Schiff base when vanillin reacts with the paramino groups of procaine. Cocaine remains colorless when vanillin is added. One gram of vanillin in one liter of procaine hydrochloride will produce a moderately deep yellow color which is neither changed nor destroyed by autoclaving. The stain is readily washed from hospital linen. It does not tattoo the skin of human beings or rabbits, rats, guinea pigs, or dogs. The vanillin however in this concentration—1 Gm. in 1 liter of procaine—renders 1.74 Gm. of procaine unavailable for anesthesia. This reduces a 0.50 per cent solution to 0.33 per cent, a 1 per cent solution to 0.83 per cent, and a 9 per cent solution to 1.83 per cent. The toxicity of vanillin is very low. Deichmann and Kitzmiller<sup>2</sup> found the minimal lethal dose of vanillin by mouth for rabbits to be 3 Gm. per kilogram of body weight. When administered subcutaneously 2.6 Gm. of vanillin per kilogram of body weight killed half of the rats tested. A single instance of sensitivity to vanillin has been reported in which eczema appeared in a worker who was not sensitive to the natural product. It is probable that other cases might appear if vanillin were injected into the skin and subcutaneous tissues.

The best dye that we have found for staining procaine is ponceau 8 X (Food, Drug and Cosmetic Red N. 4). A stock solution is made by dissolving 1 Gm. of the dye (88 per cent pure) in one liter of normal saline solution. This solution will not deteriorate. A volume of 20 c. of this stock solution added to 1 liter of procaine—a 1:50,000 solution of the dye—imparts a brilliant pink red color which is distinctively different from the color of any other solution used in the operating room. Repeated autoclaving does not destroy or change the color and the dye is not removed by filtration through paper. The light pink stain in linen or clothing washes out readily. It does not tattoo the skin or the subcutaneous tissues. No side- or aftereffects have ever been noted even though it has been used in those parts of the body where local anesthesia is indicated. The pink red color is readily discernible in a flask, in an aluminum, agate, or glass container and of greater importance to the surgeon a vivid color is readily apparent in the syringe at the beginning of and during the injection (Fig. 6).

#### PROCAINE TEST PAPER

The reaction of paradimethylaminobenzaldehyde with sulfonamides depends upon the presence of the primary amine group. This reaction was recognized and employed by Kuhnau<sup>3</sup> in developing a colorimetric method for the determination of sulfonamide blood levels. Mackee and associates have described a reagent, using the same principle to stain sulfonamides present in histologic sections. Since procaine also contains this primary amine group, we can expect a similar reaction between the benzaldehyde and procaine.

A stock benzaldehyde solution was made by dissolving 0.5 Gm. paradimethylaminobenzaldehyde in 500 c. of water to which 5 c. of concentrated sulfuric acid had been added. Slight heating may be necessary to bring all of the benzaldehyde into solution. This stock solution is light-stable though autoclaving has a deleterious effect. When procaine is added to this benzalde-

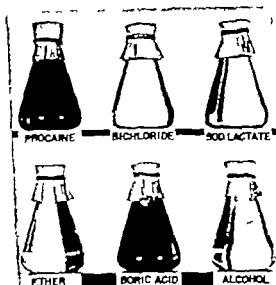


FIG. 2.—Testing solutions commonly used in the hospital and upon living tissues in order to reduce their accidents and reactions which has occurred as the result of the injection of the wrong solution.

FIG. 3.—When a solution of red liquid procaine comes in contact with our procaine test paper, an effluvia color is formed. If the surgeon is using the chloroform solution, the test should be made (as shown) before the injection by aspirating from the syringe onto the test paper.



hydro-sulfuric acid solution a brilliant yellow color is formed. It was felt however that the use of a test paper would be simpler than a test solution. Using this same principle procaine test papers were made in the following way:

A half package of filter papers, about 23 sheets, is securely held together at the periphery with a metal or plastic paper clip, photographic print holder or a spring type clothespin. After being immersed in the benzaldehyde stock solution, the papers are hung up to dry. The drying can be hastened by using an infrared lamp or a photographic dryer. When the papers are wet they must be handled by the clip, for contact with the skin causes yellow discoloration of the papers. When dry they may be handled with the dry hands cut to size suitable for storing either in boxes, bottles, or envelopes.

When plain or the pink red tinted procaine solution comes into contact with the benzaldehyde test paper a vivid yellow color is formed (Fig. 6).

We thought that the paper tops which are commonly used to cap small flasks of procaine might serve well as a test surface. Since autoclaving causes partial disintegration of the benzaldehyde solution, the resulting color reaction is delayed and of low intensity. After the procaine has been autoclaved and allowed to cool, the paper caps can then be painted with a 5 per cent alcoholic solution of benzaldehyde, which is made in the following way: 2.5 Gm. of benzaldehyde are dissolved in 50 cc. of 95 per cent alcohol to which there has been added previously 1 cc. of concentrated sulfuric acid. This alcoholic solution is excellent for painting caps for it wets the paper more readily than the aqueous solution. It also carries a greater concentration of the benzaldehyde and dries more quickly. Paper caps thus painted act well as a test paper. This alcoholic solution can also be used to paint the etched circular surface on the side of flasks. A few drops of procaine (plain or tinted) squirted against this area will produce the characteristic yellow color. Adhesive tape cannot be wet sufficiently well to act as a testing surface.

#### IDENTIFICATION OF ALCOHOL

Alcohol will produce necrosis and slough if injected into the skin or subcutaneous tissues (Figs. 3, B and 4, A). The possibility of injecting alcohol in error is ever present since the fluid is used frequently not only on the clean-up tray but also on the instrument stand at the beginning of and during the operation. If an alcohol moistened sponge is used in an operative wound, coagulation of the surface protein and death of cells occur. While physicians may be reluctant to admit openly mistakes and failures, amazing stories are sometimes related in privacy. The following episode may better illustrate this point.

A young woman, the mother of several children, as advised to have dilatation and curettage because of menstrual abnormalities. Having been admitted to the hospital the day prior to the scheduled operation, she was taken to the operating room early the following morning. The surgeon was late in arriving and in order to save time he instructed the house officer (assistant) to proceed with the spinal anesthetic while he scrubbed. Satisfactory anesthesia obtained and the operation was soon completed. When recovery of motor function and sensation in the legs had not returned in twenty-four hours, the dressing was removed from the patient's back. The tissues surrounding the point of puncture were

gray green in color and surrounded by wide zone of erythema. A large sloughing wound developed and the paraplegia remained. Whether the necrotizing solution injected in error was alcohol or some other sclerosing agent, was not known.

By this unfortunate but avoidable accident four careers were profoundly affected—those of the patient, the operating surgeon, the house officer assistant who injected the solution, and the attending nurse who filled the syringes. Who was to blame? It would appear that this catastrophe could have been avoided had the safeguard described here been observed. We have wondered whether or not other instances of paraplegia following spinal anesthesia might also have been due to the injection of alcohol or some other antiseptic or cleansing agent.

Alcohol can be tinted a fluorescent green in the following way. A 1 per cent aqueous solution of sodium fluorescein is prepared. 100 cc of this concentrate added to 100 gallons of alcohol will produce a yellow-green fluorescent solution. However, a preferable profound green and this color may be obtained by the addition of 50 cc of a 5 per cent alcoholic solution of brilliant green. This amount of the dye in alcohol will not stain the skin. The faint green tint in linen will readily wash out since the dye is water soluble. This same dye is used by some manufacturers to tint cosmetic preparations such as hair tonic and after-shaving lotions (Fig 5). Employed extensively at the Duke Hospital and the Johns Hopkins Hospital for many years, this dye has caused no observed cases of sensitivity.

#### IDENTIFICATION OF BORIC ACID SOLUTION

Despite the widespread use of boric acid, poisoning resulting from its use is relatively uncommon. Toxic manifestations arise usually from application of the drug to large areas of high absorbing power and may occur in the wet dressing of burns, irrigation of large cavities, ingestion, or accidental administration by injection as reported by Leyton and Green. In their patient, a hypodermoclysis of normal saline solution was ordered, but in error the patient received 700 cc of 4 per cent boric acid solution which represented an intake of 28 Gm of boric acid. The diffuse edema which developed was followed by desquamation. There was marked abdominal distention, nausea, vomiting and intractable abdominal pain. There occurred a period of disorientation and confusion due to impaired renal function. Subsequently the blood and urine chemistry returned gradually to normal with improvement in the patient's general condition. The patient developed colon bacilli pyelonephritis despite continuous excretion of relatively large amounts of borate in the urine. This may be a commentary on the effective excretion of boric acid as an antiseptic.

The error just described could have occurred in the pharmacy or central supply room when the original solution was made. What seems more likely, however, is that an innocent house officer in a haste to administer urgently needed fluids, selected the wrong bottle, without careful reading of the label. Since boric acid is colorless and similar in appearance to glucose and saline solutions, a dye should be added to safeguard the patient and physician and to prevent a repetition of these accidents. This may be accomplished in the following way.

A concentrate may be made by adding 8 Gm of amaranth and 2 Gm of brilliant blue to 1 liter of distilled water. A volume of 10 cc of this concentrate is added to each 20 gallons of 4 per cent boric acid. The solution is then filtered. The resulting tinted solution of boric acid is a vivid lavender which is readily distinguishable from all other solutions commonly used in the hospital. The color is heat and light-stable and remains unchanged after autoclaving.

#### PREPARATION AND IDENTIFICATION OF SODIUM LACTATE

While we know of no instance of fatality resulting from the improper use of sodium lactate solution, an indicator dye is, nevertheless, necessary not only to identify the solution, but also to indicate the pH of the solution. Acidic solutions of sixth-molar sodium lactate will produce necrosis and slough (Fig 3 B). Accidents with such material can be prevented by preparing the colored lactate solution in the following manner:

An aqueous stock solution of 0.05 per cent phenol red is prepared. This indicator dye is yellow at pH 6.8 and pink violet at pH 8.4. A volume of 6.8 cc of the stock solution is added to 4 liters of molar lactate which, on further sixfold dilution to make sixth molar lactate, will become yellow-orange in color. The solution is then boiled for several hours over a low flame and 5 per cent sodium hydroxide added slowly until the solution changes in color from the acid yellow-orange to the basic pink violet. If the pink violet color reverts to yellow-orange during autoclaving an insufficient amount of sodium hydroxide was added to complete the reaction. Only the solution which is violet in color indicative of a basic reaction should be used. The acidic solution will cause necrosis and slough (Fig 3 B).

#### IDENTIFICATION OF ETHER

Because of its volatility and low boiling point ether will spout from a syringe which is held in the hand for several minutes. Since it evaporates rapidly a few drops on the gloved or bare hand disappears quickly and will produce a cooling sensation. In spite of this however a syringe filled recently and pressed rapidly to the surgeon might be injected in error (Fig 3 A).

A volume of 0.1 Gm of *p*-dimethylaminazo benzene (butter yellow) added to 1 liter of ether will color the solution a brilliant yellow (Fig 3). This compound is also soluble in alcohol but is insoluble in water.

#### IDENTIFICATION OF MERCURY BICHLORIDE

The *Pharmacopoeia of the United States* states that poison tablets of mercury bichloride must be of a distinctive color not white; they must be of an angular or irregular shape not discoid. This directive was issued to make mistakes less liable. Among the popular shapes used by manufacturers are oblong, rectangular coffin-shaped, and triangular. The blue color is due to the addition of indigo carmine.

Mercury bichloride tablets are usually manufactured in 0.5 Gm weight although a 4 Gm size can be obtained. One 0.5 Gm tablet added to 475 cc (one pint) of water will make a 1 to 1,000 solution. A solution of bi chloride

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ery distressing one. The tinted solutions and the procaine test papers are added safeguards for the surgeon who is responsible for his patient and liable if an accident occurs.

The tinted solutions and the procaine test paper here described have been used for more than two years at the Duke Hospital without deleterious effect.

#### CONCLUSIONS

1. A procaine test paper is presented which will identify and distinguish procaine from other substances commonly used in the operating room.

2. Procaine is tinted pink red by the addition of ponceau 8 X which will neither tattoo the skin nor stain linen. Of greatest importance to the surgeon this vivid color is readily apparent in the syringe at the beginning of and during the injection.

3. Alcohol is tinted green by the addition of fluorescein and potassium carbonate.

4. Ether is tinted yellow by the addition of p-dimethylaminoazo benzene (butter yellow).

5. Boric acid is tinted lavender by the addition of amaranth and brilliant blue.

6. Methods of preparing sodium lactate and mercury bichloride are presented.

The authors are grateful to M. Thomas Retamer, Pharmacist of Duke Hospital, and to Mr. Alex. Oetting, Pharmacist of the Johns Hopkins Hospital, for their helpful suggestions.

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in this concentration which is most commonly used is deep blue in color (Fig 5). When diluted, however, the color changes from a vivid blue to sea green. This reaction also occurs when the surgeon washes bloodstained gloves in it. Since blebchloride incites a marked local tissue reaction, the gloved hands should be either wiped dry or rinsed in physiologic saline solution before re-entering a wound.

#### DIFFERENTIATION OF COCAINE AND PONTOCOCAINE

A saturated solution of potassium permanganate added in approximately equal volumes to cocaine, pontocaine, and procaine will form a brilliant violet crystalline precipitate with cocaine while a dirty muddy solution will result with pontocaine and procaine. Procaine can be distinguished from pontocaine by the use of the procaine test papers described in the preceding pages of this article.

#### SUMMARY

Despite its simplicity and safety resulting from the administration of local anesthetic agent and parenteral fluids have undoubtedly been more numerous than one would be led to believe from the few isolated cases which have been reported. While this may be construed as indicative of the infrequency of such accidents, no otherwise, it is more likely due to a failure to publish them. Physicians are always eager to report successes, but are equally reluctant to record failures or mistakes.

We believe that more accidents and reactions occur as the result of injection of the wrong solution, or one improperly prepared, than those due to sensitivity to the agent. When a physician has had the misfortune of administering the wrong solution, and a severe reaction has ensued he is of the opinion, and perhaps rightly so, that he would be blamed for the accident, and so it has seemed to him that no good purpose would be served by reporting it. Thereby the custom has grown up of not recording these accidents, although a service might have been rendered by repeatedly calling to the attention of the medical profession the possibility of mistakes, and emphasizing the need to safeguard in an effort to prevent them. It was with this idea in mind that the present study was undertaken, since we were unable to find reference in the medical literature to any work on this problem. Discussion may stimulate further investigation which may lead to better prophylaxis.

The migration of student and graduate nurses through the various operating rooms has enhanced the possibility of the surgeon being given a syringe containing the wrong colorless solution. Substitution accidents may occur in several ways. The error may have been made in the pharmacy where either the wrong or an improper solution was made, the final package was improperly or incompletely labeled and identified. Of more frequent occurrence in our opinion is the error made by the nurse, the house officer or the surgeon himself who having several colorless solutions, such as alcohol, ether, procaine, saline, etc. on the instrument tray may draw into the syringe the wrong solution for injection. While this error may seldom occur when it does the result may be a

a crushing type of fracture more commonly result in ankylosis than a simple fracture through the condylar neck.

A few cases, such as the one of Burket and those of Blackstone (Wakeley<sup>14</sup>) have been recorded wherein bony union was present at birth. As the earlier the onset the greater the deformity these are of particular interest from the therapeutic standpoint. Our Case 2 was such a problem.

In adult life trauma is the most frequent cause of bony union as Blair has pointed out. In this age period relatively more of the extra-articular ankyloses occur. Fibrosis of the masseter or internal pterygoid muscle due to infection, as in osteomyelitis, actinomycosis, or noma, or due to external trauma as with war wound or like trauma, will produce inability to open the jaws even to the extent of simulating true ankylosis. The same result is obtained with irradiation fibrosis, carcinomatous invasion of these muscles, or the contraction of the skin of the face or mucous membrane of the neck following thermal or chemical burns. Wounds produced by war missiles have caused bony union and considerable fibrosis of the soft tissues, complicating the picture. Prolonged muscle spasm and disuse atrophy with fibrosis have been reported as causes of pseudo-ankylosis.

#### PATHOLOGY

A solid block of bone quite hypertrophic is usually found at operation for true ankylosis. This may often obscure the normal landmarks so that the condylar head, glenoid fossa, articular eminence and anterior wall of the external auditory canal cannot be distinguished. Not infrequently this bony mass often runs the sigmoid notch to the coronoid process which may be fixed laterally to the zygomatic area and medially to the maxillary tuberosity. In growth of this kind, which is more common in children, especially in the recurrent cases where osteogenic activity is great, invites the danger of entering the middle cranial fossa or the ear canal.

In early cases fibrous band alone may be found obliterating the joint space. Rarely is the disc identifiable. Ossification takes place rapidly as can be seen in waiting recurrences developed after operation.

In children, retardation of mandibular growth results from disuse and interference with the ossification center in the condylar head. The younger the child at the onset the greater is the deformity. The ramus and body of the mandible on the affected side are small causing the him to retude and more nearly normal growth from the opposite side produces a lopsided facial defect with an elongated flattened normal side and a fuller but shorter involved side. Due to disuse and improper relationships, severe arches and malocclusion with deviation and overbite develop.

Occasionally limitation of opening is present with abnormal development of the condylar head without true or false ankylosis as in Case 1<sup>st</sup>. Usually here the head is large but the neck, ramus, and body are short and underdeveloped. The large head is unable to follow the condylar articulation so that opening stops after 1 to 2 cm. Although there is marked receding chin in these cases and deviation to the affected side if the pathology is unilateral.

# ANKYLOSIS OF THE TEMPOROMANDIBULAR JOINT

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**O**RGANIC fixation of the jaw is most commonly due to bony ankylosis of the temporomandibular joint infection and trauma being the common predisposing causes. Extra-articular fibrosis does not occur as frequently a bony union but accounts for about one-third of all cases. When fixation develops in childhood, the deformity is more severe. Development of the mandible, face and teeth is interfered with as well as general development due to faulty nutrition and speech. Wide resection of the condylar head and neck gives the best permanent results in cases of true ankylosis. Muscle fibrosis and trismus as in pseudo-ankylosis may be overcome by stretching but with marked fibrosis and scarring the addition of soft tissues and oral lining may be necessary to give adequate opening.

Since Humphry in 1854 reported the first successful operation for ankylosis of the temporomandibular joint there have been many reports of a few cases but only a few surgeons have had sufficient numbers of this deformity to analyze their results with statistical meaning. The largest series were those of Dufourmentel and Darrozeau with 100 cases, Karyajan with 33 and Blair with 18. As the disease entity is rare enough to justify many one-case reports and as the literature contains only about 31 published cases (1 in 1936 according to Loop) our consideration of 22 cases seems warranted.

## ETIOLOGY

Most common among the causes of ankylosis have been reported infection and trauma. As many authors have discussed intra- and extra-articular pathology together Dufourmentel and Darrozeau discuss only the etiology of bony ankylosis alone gives the best analysis for that purpose. In their 100 cases, the cause was listed: unknown in 29 due to trauma in 2, due to histrietal for cephalic injury in 5 and accounted for by infection in the remaining 41. Of this largest group, infection 10 were due to gonorrheal arthritis, 9 to infection of dental origin, 8 to otitis media, 5 to arthritis with measles, 3 to arthritis with scarlet fever, 2 to arthritis with diphtheria and with typhoid fever, and 1 each to tuberculosis and to trauma. In most of the large group of unknown causes, a history of difficult labor was obtained and trauma was thought but not proved to be the cause. Many of this group were considered normal babies until the ages of 1 to 18 months when solid foods were introduced into the diet progressive difficulty in opening the mouth was noticed. In the dental known trauma group of 10 a falling of the external auditory canal was noted in each case. Dufourmentel and Darrozeau stated that if the articular surface of the joint had not been broken there was ankylosis. According to Hellbracer

Read at the meeting of the Society of American Surgeons, New Orleans, La. Jan. 29-31, 1948. †Deceased. This paper is in preparation. The thesis of Dr. Padgett on this

between the cut bone end has been the subject of debate but adequate resection is the requisite of success.

Exposure of the joint is difficult because of its depth and because of the vascularity of the region. A slightly curved incision 3 cm. long and 1 cm. in front of the tragus is adequate. It should start in the hair just in front of the helix and curve downward and backward (Blair). A T incision with the horizontal run over the zygomatic process of the temporal bone is favored by some surgeons (Wakeley). The skin flap is retracted anteriorly only a short distance to avoid the upper branches of the facial nerve, and the auriculotemporal nerve and superficial temporal artery are avoided posteriorly. After the wound is deepened to the condylar neck, which is bared by a periosteal elevator with a chisel the neck is cut through, avoiding the internal maxillary artery which lies just beneath and which if cut will bleed, obscuring the field. Suction through a small tip will aid dissection by better vision. If the artery is cut, a plug will usually be sufficient to stop the bleeding. The bone may also be cut through by a high saw (Wakeley) a self-stopping skull drill (Henry<sup>14</sup>) or up biting Harrison rongeurs. The upper portion of the bony mass is avoided as there are no landmarks and the middle cranial fossa could easily be opened. With rongeur and chisel the bone should be cut through well down on the ramus (see Fig. 1) so that at least 1.5 cm. or better a 2 cm. gap results. A drain or pack inserted for bleeding should be removed in twenty-four to forty-eight hours.

Much has been written to the effect that the interposition of some substance is necessary to prevent re-ankylosis. Autogenous tissues such as cartilage, muscle or fascia have been used frequently as well as foreign materials, chiefly inert metals. Good results have followed cartilage insertion (Blair<sup>2</sup>) Dufourmentel, and Darenbourg<sup>15</sup> but it is not unlikely as Blair pointed out, that the cartilage best served to fill up the dead space after adequate resection which chiefly was responsible for the lasting result. Temporal fascia as advocated by Wakeley and Henry, or fascia lata as used by Kojanjiun<sup>1</sup> have been utilized with apparent good results but the fascia has been shown in some cases to be absorbed or worn through quickly. Foreign materials such as the tantalum foil used by Eggers<sup>16</sup> may give the desired result but might also set up irritation in its infection and be extruded. We placed a tantalum cup over the sectioned condylar neck and have to date after one and one-half years, a well functioning jaw.

When the coronoid process is involved in the ankylosis, it must be sectioned as must any attachment of the ramus to the zygomatic arch or the maxillary tuberosity. Brown and associates<sup>4</sup> pointed out that the temporal muscle should be freed completely from the coronoid process before it is severed. If there is a large bony mass producing solid union involving the coronoid process, the sigmoid notch, and the condylar head and neck, it is easier and less formidable to perform the operation of Reddon, that of cutting a row the ramus to produce a gap and false joint. This procedure was done in our Cases 10, 11 and 12 with good results.

Surprisingly after removal of the condylar head and neck and portion of the ramus, open bite does not occur as would be expected. After such a resec-

## DIAGNOSIS

With the marked recession of the chin and deviation of the jaw toward the affected side the diagnosis is easy in long standing cases of unilateral involvement since childhood. The most obvious deformity is on the normal side, which is misleading to the uninformed observer. There may be as much as 5 mm. of opening between the incisors but usually less. Occlusion is poor with all the teeth on the unaffected side in improper relationship with the opposing maxillary dentition deviating toward the affected side. There is a marked tendency toward an overbite with the mandibular development. The preangular notch is deepened on the affected side and atrophy of the masseter is more definite on the side of the ankylosis. Caries are common in cases of long standing.

Attempted active movement and forceful manipulation may help establish the differentiation as to the side involved in adults. Some forward motion can be seen and felt when the patient tries to open the jaws but the movement is only on the normal side, the ankylosed side remaining fixed. Bilateral ankylosis allows no motion at all. If forceful opening produces pain at a certain point, a false ankylosis is more likely present. True ankylosis gives no pain with this procedure. Fibrous bands and scars may be obvious but if the pathology is chiefly inside the mouth in the buccinator or internal pterygoid regions, forceful opening under anesthesia will likely be necessary to determine their presence. This was true in two of our recent cases (not reported here) with carcinomatous invasion of the internal pterygoid muscle from an alveolar margin epithelioma. Following severe facial injuries there may be bony union on one side and a fibrous ankylosis on the other obscuring the diagnosis.

X-ray examination is helpful but not so diagnostic as the clinical signs. In early cases and in those with pseudo ankylosis, little or nothing can be learned from the roentgen picture. The earliest changes seen are simply indefinite outlines of the condylar head and glenoid cavity. Both sides must always be taken for comparison but difficulty in interpretation always comes up because of this indistinctness. The technique of obtaining sharp outlines of the normal joint is not easy. Slight errors in positioning for the picture will superimpose shadows of over or underlying structures on the joint outlines. Even after careful study of films with the roentgenologist the reported wrong side has been operated upon first by some. This error occurs more often in adult whose ankylosis has come on after maturity the signs of the side involved being less obvious without growth changes. Advanced cases, as in Case 11 show massive hypertrophy of bone obliterating the sigmoid notch. The largest bony overgrowths are seen in children with recurrent ankylosis following operation.

## TREATMENT OF TRUE ANKYLOSIS

Restoration of function is the first consideration of treatment cosmetic improvement being secondary. In most cases of bony ankylosis wide resection of the condylar neck and adjacent portion of the ramus will produce adequate motion of the lower jaw. Most of the recurrences have occurred because the bony gap was not made wide enough. The interposition of various values here

and with only two recurrences, both times when the cartilage had become infected and was lost. Recurrence of ankylosis, when it occurs, will be evident by the end of six months after operation.

#### TREATMENT OF FALSE ANKYLOSIS

The treatment of extra-articular fixation presents a more difficult problem. The binding scars or muscle fibrosis must be overcome. Stretching has been frequently attempted and many ingenious dilators which are helpful in some cases have been devised. Frequent forceful openings under anesthesia may be indicated, the jaws being kept open by wiring between the molars a wooden block which is left in place two to six weeks. This has been our method of choice. The insertion between the teeth of rubber keys of increasing sizes may be helpful. Berger used a screw wedge and a holder. Advocated several devices including hard rubber screws, clothing pins and mechanical dilators. Forceful manipulation in early true ankylosis should not be done as it will likely speed the formation of bone.

When repeated forceful openings have failed, surgery is indicated. The scars and muscle fibrosis which inhibit opening of the jaws must be cut across or excised and the defect covered by new tissue. Binding scars of the cheeks externally can be removed and the surface defect easily covered by a skin graft. If the defect is large and a more fill-out contour desirable, soft tissue may be added in flaps from the neck, lower upper arm. Flaps are better than skin graft if much of the muscle must be removed. For the loss of buccal mucosa with contracture a satisfactory coverage as was used in some of Blair's cases is a new living split-skin graft. In the Escherich method. These skin grafts should be 50 per cent larger than expected to allow for the subsequent contraction. The results in the extra-articular cases will usually be less dramatic than in true ankylosis.

#### COMPLETE CO-ADAPTATION

After restoration of motion of the jaws, cosmetic considerations are indicated for the distorted face and receding chin. Large cartilage implant from the costal margin inserted alongside the body of the mandible and in front of the hyoid from below give the best results. Blair has lifted the jaw around after condylar resection and wired the teeth in better occlusion with considerable improvement. Kazanjian has cut the mandible in an oblique or L-shaped fashion through the ramus and body and, after reducing the affected side anteriorly, fixed the teeth in a better occlusal relationship. It would seem logical that sliding operations of this type requiring long fixation not be attempted for several months because of the chance of recurrence of the ankylosis.

#### CASE REPORTS

##### Analysis of Cases

Of our 22 cases, 16 were true ankylosis, were false due to extra-articular fibrosis, and 1 was caused by developmental abnormality of the jaw. In 2 of the long unions the coronoid was also involved. Late follow-up was adequate in 16 of the 22 cases but 6 were untraceable. Many of our patients were service

tion it would seem logical for the molars to hit first on closure of the jaws and the incisors to hit later or not at all but no such fulcrum action results.

Early and continued motion after operation, contrary to the opinion of Alphon and Brooks, is beneficial although some men, Kazanjian<sup>17</sup> and Eggers<sup>18</sup> advocated rest for one week postoperatively. We agree with Campbell<sup>6</sup> that motion should begin at once with the jaws opened to their full excursion daily. Opening is relatively painless and the patient is delighted from the first day to find that jaws so long fixed can be opened. Mechanical aids such as Darre's<sup>19</sup> automobilizer and others are unnecessary following surgery for true ankylosis. Everyone is agreed that frequent active exercises are of value. Full opening daily and frequent gum chewing will give the necessary exercise.

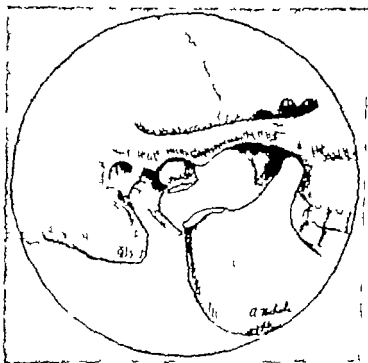


Fig. 1.—The amount of the condyle area, which is required for ankylosis, frequently exceeds the amount in the diagram.

There will be a certain percentage of recurrence, especially in the younger age group. Dufourmentel and Darre<sup>20</sup> 100 cases had perfect cures in 6 wherein there was an opening of 1 to 3 cm. but 9 of these patients needed reoperation because the resultant opening was less than 1 cm. After one recurrence the prognosis is worse for a good result from the next could far removal and the mass of recurrent overgrowth in children may make a ramus or body resection necessary instead of further surgery in the joint region. Dufourmentel and Darre<sup>20</sup> implanted cartilage after resection in thirty-three



D



E



F



G

FIG 2 (Cont.)—D Seven years  
posterior of kyphosis; arrow points  
F nine months after rhinoplasty operation  
rhinoplasty operation.  
After and opens low, showing maximum opening. (H  
kyphosis) (H) hypergraph) of treatment. (H) head  
the mouth can be full opened. G healed and of





Fig. 2 (Case 11).—A. Preoperative opening of the jt. B. postopera. opened first operation. C. X-ra. preoperative, first operation, showing signs evidence of the joint with early ankylosis.

		History of operation	Findings	Healed	Roentgen
11	33	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
12	34	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
13	35	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
14	36	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
15	37	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
16	38	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
17	39	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen

		History of operation	Findings	Healed	Roentgen
1	40	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
2	41	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
3	42	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
4	43	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen
5	44	Enucleation of maxilla	Enucleation of maxilla	Good	Roentgen

TABLE I

CASE NO.	AGE	AGE AT ONSET	TYPE	INTERCOURSE OF NO GAP	RESULTS	REMARKS
1	25 yr.	11 months 13	Dissection of readily retractile testis	Patent	Recurrente good re- sults and operations	Heavy uterus
2	22 mo	Maximal 1 mo	Forced manipulation re- section of readily retractile	Yess	Good	Fibrous uterus
3	31 yr	Transilluminant cervical b area 24)	Dissection of readily retractile	None	Good unobscured	Heavy uterus
4	23 yr	Dissected (section, postext ar area 1)	Dissection of readily retractile	None	Good in follow up good unobscured	Heavy uterus
5	3	Progesterone 1	Transsection lateral re- section of readily retractile	Cervical cartilage	Operative death	Abnormal joint ; heavy uterus (f)
6	23 yr	Artisanomalous, postext ar 17	Transsection lateral re- section of readily retractile	Yess	Good function distal later of antimony	Heavy uterus
7	14 1/2	Parviti 1 mo 13	Dissection of readily retractile	Patent	Good	Heavy uterus
8	10 yr	Parviti 1 mo 10 mo	Forced dilatation re- section of readily retractile	Testicular exp	Good	Heavy uterus
9	17 yr	Parviti 1 mo 10 mo	Dissection of readily retractile	Cervical cartilage	Good	Heavy uterus
10	17 1/2	Parviti 0	Artisanomalous, postext ar 17	None	Recurrente good	Heavy uterus
			Dissection of readily retractile	Yess	Good	Heavy uterus
			Dissection of readily retractile	Cervical cartilage	Good	Heavy uterus

in the office on Aug. 15, 1947 she had opening of 3 cm and normal function. Later cosmetic surgery will be necessary.

## SUMMARY

1 Temporomandibular ankylosis is relatively uncommon, warranting the report and analysis of twenty-two cases.

True bony ankylosis is most frequently caused by infection of trauma pseudo-ankylosis results from soft tissue fibrosis chiefly following burns, wounds, infection, or irradiation.

3 Pathology found at the time of surgery in early cases of true ankylosis is most often an intra-articular fibrosis but in more advanced stages a massive bony hypertrophy is present obliterating the normal landmarks.

4 Diagnosis is obvious in late cases wherein the pathologic changes commenced during childhood but is difficult as to the side of involvement in adult with a relatively short history of limitation of movement of the jaws.

5 Clinical signs are often better diagnostic aids than the roentgen examination which is difficult in technique and in interpretation.

6 Treatment of bony ankylosis is essentially wide resection of the condylar neck with removal of a portion of the condylar head and the ramus if necessary to produce a wide bony gap.

The insertion of cartilage, fascia, or inert substances to fill the gap for the purpose of preventing recurrence is of secondary and minor importance.

8 Massive overgrowth of bone especially in recurrences after resection, is best treated by cross sectioning the ramus and interposing muscle between the bone ends to create a false joint.

9 The treatment of pseudo-ankylosis is directed toward overcoming the soft tissue fibrosis. If early repeated stretching may be efficacious but if late and this usually is the case, excision of fibrous bands, scars, or muscle is necessary with coverage by skin grafts or flaps.

10 Cosmetic improvement is secondary to function. The levated chin and jaw line can be improved by implant of cartilage or by lengthening the short side of the mandible.

11 The twenty-two cases reported are analyzed as to etiology, pathology and treatment (see Table I).

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cases whose follow up was dependent upon letters from local county health officers from over the state.

An analysis of the causes revealed that 11 of the 16 true ankyloses were due to infection, 4 to trauma, 1 to unknown etiology and 1 was present at birth. Infection in the joint followed mastoiditis in 3 patients, multiple suppurative arthritis in 4, parotid abscess in 2, and osteomyelitis, erysipelas, actinomycosis, and infection of unknown cause in 1 each. In the five pseudo-ankyloses, irradiation fibrosis was the cause in 2 cases and actinomycosis, nonspecific infection and an unknown cause accounted for the other 3. In 6 patients of both types, true and false, a dental extraction immediately preceded the acute process. Mandibular maldevelopment was present in all patients when ankylosis had begun under 15 years of age.

The results of treatment were fair but not remarkable. Manipulations previously attempted on patients before they were referred to us were useless and seemed to have increased the ankylosis. Condyle resection was performed 19 times in the 17 cases of true ankylosis with failure 6 times, one patient having two recurrences. Ramus resections after Risdon gave good function in each of the 3 patients upon whom it was performed. These three were among the five recurrences.

In regard to filling the space cartilage was inserted in the gap left in the resection 3 times with 1 recurrence. Fascia was inserted 4 times with 3 recurrences. A tantalum cup over one of the cut bone ends was placed in only 1 patient who had no recurrence. Nothing was inserted in 10 cases, with 1 recurrence in which a pseudo-ankylosis was probably also existent. There was 1 operative death in the series.

In the false ankyloses strict hinging was attended with success in 1 patient. The addition of more tissue after cutting out the scars was performed in 2 patients with success.

In Table I are analyzed the 22 cases, as to etiology, pathology, and treatment.

### *Illustrative Case*

Case 11 (No. 1437B, H. C. (New Hope).—A 7 year old girl had not been able to open her mouth more than  $\frac{1}{2}$  inch for  $3\frac{1}{2}$  years following left mandibulotomy. She had been treated three previously. Other previous X-ray examinations showed some narrowing of the left temporomandibular joint with degenerative changes. On Nov. 24, 1930 the joint was explored and the residual neck cut across widely. She regained the head of the condyle being ankylosed to the sticulus foras. A flap of temporal fascia was turned down between the cut bones. A pack inserted for bleeding was removed in three days. Five days after operation she was able to open her mouth one inch and on December 15 she had attained the goal function.

The fixation of the joint recurred again within a few months but nothing done until by considerable effort we traced her and urged that she return for more surgery. She was admitted to the University of Kansas Hospital on Nov. 13, 1934, and on operation was performed the next day. X-ray examination of the joint showed large thick bony mass involving the entire condyloid region and extending to the articular process. A Risdon operation was performed, severing the ramus with right saw near the angle and the masseter and internal pterygoid muscles were sutured together between the lower lip. The jaws were held widely open for one week by means of a block. When the jaws

in the office on Aug. 15, 1947 she had an opening of 2 cm and excellent function. Later cosmetic surgery will be necessary.

## SUMMARY

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# SUPPURATIVE FASCIITIS AS THE ESSENTIAL FEATURE OF HEMOLYTIC STREPTOCOCCUS GANGRENE

WITH NOTES ON FASCIOTOMY AND EARLY WOUND CLOSURE AS THE  
TREATMENT OF CHOICE

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THE term necrotizing erysipelas was introduced by Pfeiffer in 1918 to designate a specific infection due to beta hemolytic streptococci and characterized by subcutaneous necrosis and secondary cutaneous gangrene. Early surgical incision to the limit of the subcutaneous necrosis were demonstrated to be effective in the control of the spreading infection. Meleney on the basis of his experience with twenty patients in China, confirmed the wisdom of early surgical incisions, but concluded that subcutaneous necrosis was the essential feature of the disease whereas erysipelas was an irregular coincidence. It is for this reason that the infection has been designated as hemolytic streptococcus gangrene rather than gangrenous, necrotizing, erysipelas.

The clinical picture of the disease is well known. It most commonly affects the extremities. In the foot and lower leg it usually represents a secondary infection of ulceration due to tinea pedis. Elsewhere it may follow a minor injury, pinprick or hypodermic injection. Occasionally the infection is blood-borne to an area of contusion or hematoma. There is a sudden onset of pain and swelling with or without chill. Within twenty-four hours there is a considerable phlegmon with marked erythema or frank erysipelas. Prostration is severe and the pulse is rapid out of proportion to the fever. Pain may be replaced by numbness. The pathognomonic sign of the disease has been described as a dusky hue of the skin with or without blisters or bullae and usually appearing on the third, fourth or fifth day of the infection. Before potent antistreptococcal therapy was available multiple incisions of the heat-seal type were lifesaving. The wounds were then debrided and the considerable defect pinch-grafted six to eight weeks later.

It is the purpose of this report to present certain modifications in our understanding of the disease in consequence of experience with penicillin-treated infections. In the observation on fulminant cases, Meleney's attention was directed to the subcutaneous rather than the cutaneous maximal vulnerability. He was unable to validate this concept in studies of bacterial phase formation by the etiologic organism and ultimately came to the conclusion that the disease was an anaphylactic phenomenon of the Shulz or Arthus type. In our

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studies of penicillin treated infections the subcutaneous necrosis has been limited quite clearly to a suppurative fasciitis. An adequate explanation of the special vulnerability of collagenous tissues is provided by the demonstration of the activation of a highly proteolytic serum toxin factor by streptococcal fibrinolysin. Hence it is our belief that hemolytic streptococcus gangrene is an extensive cellulitis which, even under modern therapy is frequently complicated by abscesses of the fascial planes.

Recognition of suppurative fasciitis as the essential feature of hemolytic streptococcus gangrene has simplified clinical management. The diagnosis and surgical incision should not be deferred for the appearance of the older pathognomonic sign of impending cutaneous gangrene. Recognition of persistent edema along a fascial plane in an infection otherwise subsiding under antistreptococcal therapy is indicative of a fascial plane abscess. Such abscesses have not subsided under continued drug therapy alone and, indeed a few infections have recurred when minor edema has been disregarded and treatment stopped.

The heat scratch type of incision has been discarded in favor of planned fasciotomy incision designed to expose the entire length of the fascial plane abscess. We have tried to avoid these long incisions by intensifying drug therapy and merely establishing dependent drainage. In such instances, especially in the upper extremity there has usually been progressive fascial slough. The most efficient method of avoiding long incisions is early recognition of fascial plane edema and prompt surgical intervention. After incision a fine mesh gauze is introduced into the wound and the extremity immobilized by a gentle pressure dressing.

Early secondary closure of these frequently considerable defects has proved practical and feasible. After fasciotomy the first dressing should be done in the operating room with facilities at hand for suturing the wound. It is important to allow three to five days to elapse after drainage in order that gross infection of the wound may be evaluated, the adequacy of the initial drainage. Further the wound should be closed before ten days have elapsed and fibrous tissue fixation prevent adequate tissue mobility. We have not hesitated to drain residual abscess pocket and lose clean portions of the wound at the same sitting. Penicillin and streptomycin have been continued throughout the period of surgical management.

# CASE REPORTS

CASE 1. H. N. T. 46 — T. H. 46 admitted Nov. 1, 1946. Three days previous the patient had learned he left wrist with penicillin. Paraesthesia and numbness were noted. He went four hours. Black dots appeared on the third day. He presented irritability but febrile. The paraesthesia persisted as a result of treatment for seven days. He was discharged from the local hospital with persistent drainage.

Four days previous admission Cherry Hospital the wrist became swollen again and he was treated with subsequent exacerbation of infection. The patient was known during reporting 40 units of penicillin were injected daily and had lost twenty pounds during the present illness.

On admission the patient did not appear acutely ill. The left upper extremity appeared as shown in Fig. 1. Penicillin given 50,000 units every three hours intravenous.



and surgical incision of the fascial plan abscesses as performed seventeen hours after entry. Wound cultures revealed beta hemolytic streptococci, salmonella, and staphylococcus pyogenes. Blood cultures were negative. The course can be summarized as follows: Nov. 1, 1944, admitted; Nov. 12, fasciotomy; Nov. 20 secondary fasciotomy with excision of devitalized tissue; Nov. 23, partial secondary closure; Dec. 2, completion of secondary closure; Dec. 6, penicillin at 1000 U, sulfonamides begun (see Fig. 1); Dec. 20 essentially healed, started on physiotherapy. By Jan. 17, 1947, the wound was healed, with full range of motion (Figs. 2 and 3); March 10 the patient discharged well from the follow-up clinic. He could play the fiddle well as before injury.



FIG. 1, 2, and 3.

CASE (C. H. N. 147,30654)—A W. colored washerwoman, aged 30 years, was admitted Feb. 4, 1947. Three and one-half weeks prior to admission the patient suffered comminuted fracture of the left forearm (radius). Kirschner wires were inserted through the olecranon and the proximal phalanx of the thumb to fix distal alignment. The cast on upper extremity was removed in plaster with the wires left in situ. Two and one-half weeks before the olecranon of the elbow united to the radius. Her treatment was as follows: Feb. 4, 1947, started on penicillin, 200,000 U every three hours intramuscularly and sulfonamides, 1 Gm. every four hours. Feb. 6, excision of necrotic skin and subcutaneous tissue (4 by 6 cm.) over lateral aspect of olecranon, incision of lateral fascial compartments of upper and lower arm and of medial of wrist and

partment of forearm Feb 13, second re-look at the split thickness graft of tarsus  
 defect (5 by 6 cm.) Feb 22, wound healed with mild graft. II sutures removed. Feb 26,  
 discharged to clinic. March 10 fracture solid, physiotherapy started. March 23, 1947 she  
 was seen in the chair with essentially full range of motion. The patient was lost to subse-  
 quent follow up.



Fig. 4

CASE 3 (C. H. N. T4 444290) — F B a white man, retired aged 73 years, was admitted  
 Oct 28 1947. Ten weeks prior to entry the patient became entangled in barbed wire fence  
 resulting lacerations of all extremities. These healed with the exception of one laceration on  
 the left forearm, which suddenly became swollen, erythematous, and painful. He  
 known diabetic and was immediately hospitalized elsewhere for penicillin therapy. The arm  
 improved considerably and the patient was discharged five weeks with minimal residual  
 edema over the medial and lateral compartments of the forearm. Ten days after cessation of  
 penicillin there was exacerbation of the infection and he entered Charity Hospital.

On admission the arm greatly swollen and erythematous and the patient was having  
 recurrent attack of angina pectoris. He seemed prostrated but was not acutely ill. He  
 was treated on penicillin, 50,000 units in three hours intramuscularly and diabetic  
 regimen. Within forty-eight hours the edema disappeared entirely from the upper arm, but  
 there was residual induration and edema along the medial aspect of the forearm. Subsequent  
 course was as follows: Oct 30 1947, recovery of medial and lateral compartments of fore-  
 arm. Nov 1, partial return of skin defect. Nov 12, all wound dry daily stellate blocks  
 for three days. Dec 1 discharged healed.

and surgical incision of the fascial plane abscesses, as performed seventeen hours after entry. Wound cultures revealed beta hemolytic streptococci, salmonella, and staphylococcus pyogenes. Blood cultures were negative. The course can be summarized as follows: Nov 12, 1946, admitted; Nov 13 fasciotomy; Nov 20 secondary fasciotomy with excision of devitalized tissue; Nov 25 partial secondary closure; Dec 2 completion of secondary closure; Dec 6, penicillin stopped, sulfamonomides begun (see Fig. 3); Dec 20, essentially healed, started on physiotherapy. By Jan 17 1947 the wounds were healed, with full range of motion (Figs. 3 and 4); March 10, the patient was discharged well from the follow up clinic. He could play the skills as well as before injury.



Figs. 1, 2 and 3

CASE 3 (C. H. N. 14 25066) — A. W. (colored) Johnson, aged 50 years, was admitted Feb. 4, 1947. Three and one-half weeks prior to admission the patient suffered comminuted fracture of the left forearm (radius). Kirschner wires were inserted through the olecranon and the proximal phalanx of the thumb to fix distal alignment. The entire upper extremity was then encased in plaster. He was left in cast. Two and one-half weeks before entry and one week after fracture, his arm became swollen and painful about the olecranon. The cast was partially removed and revealed marked swelling in the region of the elbow. The lesion developed progressively cutaneous gangrene and the patient was admitted to the Orthopedic Service of the Charity Hospital. He was seen at the Surgical Service, where treatment was as follows: Feb. 4, 1947, started on penicillin 30,000 units every three hours intramuscularly and sulfamonomides, 1 Gm. every four hours. Feb. 5, removal of necrotic skin and subcutaneous tissue (4 by 8 cm. on lateral aspect of olecranon, incision of lateral fascial compartment of upper and lower arm and of medial fascial com-

parietal of forearm Feb 1 secondary lower 1/4 split thickness graft of cutaneous defect (5 by 6 in) Feb 11 wound healed with table graft all sutures removed Feb 20, discharged to home March 10 fracture healed, physiotherapy started March 28, 1941 she was seen in the clinic with essentially full range of motion The patient was lost to subsequent follow up.



Fig 4

CASE (CHN) T. 19350 — F B, white female, aged 3 years, admitted Oct 27 1941 T 101.0 prior to entry the patient became entangled in bedclothes with fever containing larvae and flies in the rectum These healed with the exception of one laceration on the right forearm which suddenly became swollen, erythematous, and painful H was known diabetic and was immediately hospitalized elsewhere for penicillin therapy The response was considerable and he patient was discharged after one week with unusual residual edema over the medial fascial compartment of the forearm T 101.0 after cessation of penicillin here as exacerbation of the infection and he entered Charity Hospital.

On admission the arm greatly swollen and erythematous and the patient was having recurrent attack of angina pectoris H seemed prostrated but was not acutely febrile H started on penicillin, 50,000 units every three hours intramuscularly and diabetic regimen Within forty eight hours he almost disappeared entirely from the upper arm, but there was residual induration and edema along the medial aspect of the forearm Subsequent course was as follows Oct 30 1941 1 incision of medial and lateral compartments of forearm Not partial suture of skin defect Nov 15, 11 wound dry daily stellate blebs for three days Nov 14 discharged healed

Case 4 (C. H. N. 44-129 604) —H 31. A 41 year old man, retired, got well again, was admitted Aug 1, 1941. This patient developed an acute erythema, red painful swelling of the left arm and was admitted to another hospital thirteen days prior to entry. He was treated with penicillin but developed an area of skin gangrene at the elbow. This began to drain spontaneously and the patient was then referred to Charity Hospital. He was given 100,000 units of penicillin at three hour intervals and blood transfusion. Eight hours after entry he was taken to the operating room. Subsequent course was as follows: Aug 19, 1941, medial and lateral fasciotomies of upper arm and forearm; necrotic tissue was excised; penicillin therapy continued. Aug 24, secondary suture of lateral fasciotomy incision and further drainage of the anterolateral space. Sept 5, medial fasciotomy incision sutured. Sept 19, wounds healing kindly; Oct 3, all wounds healed except minor area in anterolateral fossa not previously sutured. Oct 7, he was discharged to the home. Oct 22, all wounds were healed and there was complete range of motion.

#### CONCLUSIONS

1. As a consequence of experience with penicillin treated infections, suppurative fasciitis and fascial plane abscesses appear as the essential features of hemolytic streptococcus gangrene.

Residual edema along fascial planes in an otherwise subsiding infection is an indication for planned fasciotomy and surgical drainage of the fascial plane spaces.

3. Early secondary suture of the fasciotomy is entirely practical and minimizes deformity.

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- A Physiological Approach to the Local Treatment of Burns—Edward L. Howes, Columbia University College of Physicians and Surgeons  
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 The Local Effects of Polyplythim on Malignant Tumors—P. E. Krael, Medical College of South Carolina.

The presidential address by Robert Zollinger to the annual dinner was concerned with the important and pressing problem of post-war trends in the training of general surgeons. A resolution passed by the Society concerning the untimely death of Elliott C. Cutler follows.

JANUARY 20, 1919

#### Resolution

WHEREAS Since our last meeting we have suffered the loss of a beloved and honored member and inspiring teacher of surgery Elliott C. Cutler and

WHEREAS The Society of University Surgeons can serve no higher professional and moral ideal than those which Dr. Cutler furthered in his own life and work,

THEREFORE BE IT RESOLVED That the Society of University Surgeons hereby formally expresses its deepest regret to Dr. Cutler's death, and hereby rededicates itself to service of the cause for which he so effectively labored,

AND FURTHER THAT A copy of this resolution shall be sent to Mrs. Cutler and copy published together with the proceedings of this session of the Society.

# SURGERY

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No. 3

## Original Communications

### Society for Vascular Surgery

#### VENOUS THROMBOSIS

ALTON OCHSNER, M.D., NEW ORLEANS, LA.

(From the Department of Surgery, School of Medicine, Tulane University of Louisiana, and the Ochsner Clinic)

IT IS with some trepidation that I speak on venous thrombosis before this assembly because I am well aware of the splendid fundamental investigations in this field which have been conducted by many of the members of this organization. The contributions of Hottel, Allen and associates, Bancroft, de Takats and Fowler<sup>1</sup> and many others have added much to the present-day knowledge of this distressing, frequently dangerous, and usually disabling condition. Fortunately at the present time because of a more thorough understanding of the underlying pathologic condition in venous thrombosis, much can be accomplished in preventing the occurrence of intravascular clotting and in treating the condition rationally once it has developed.

#### TYPES

Although there are some who will not agree with us, we are convinced from our experimental and clinical observation that in order to understand venous thrombosis correctly and to treat it rationally and satisfactorily it is necessary to differentiate two types of thrombosis, thrombophlebitis and phlebothrombosis, which are alike only in the respect that in both the lumen of the vein contains a clot. These two types of venous thrombosis differ in etiology, pathology, clinical manifestations, prognosis, and therapy. Unless distinction is made between the two types, the therapeutic results are likely to be unsuccessful. Thrombophlebitis, as the name implies, is a condition in which there is inflammation of the venous wall associated with an intravascular clot whereas phlebothrombosis is characterized by an intravenous clot unassociated with an inflammatory process in the venous wall. The presence of the inflammatory process in thrombophlebitis but its absence in phlebothrombosis is of great prognostic and therapeutic significance.

Presidential address delivered at the first annual meeting of the Society for Vascular Surgery, Atlantic City, N. J., June 3, 1947.



The clotting in thrombophlebitis is a result of injury to the vascular endothelium from mechanical trauma, invasion of the perivascular lymphatics by bacteria or their toxins, or chemical injury; whereas in phlebothrombosis, the intravascular thrombus is due to alterations in the cellular and fluid constituents of the blood which increase the clotting tendency and to venous stasis. In thrombophlebitis the clot resulting from injury to the endothelium is firmly attached to the wall of the vessel and does not become detached except in the presence of suppuration; for this reason there is little or no danger of embolism. Moreover because of the inflammatory process in the venous wall, impulses originate in the vein which are carried over the sympathetic nervous system to the ipsilateral arterioles, resulting in profound arteriolar spasm and edema which may persist and cause prolonged disability. On the other hand, in phlebothrombosis without inflammation of the vein the clot is a coagulation thrombus, is only loosely attached to the venous wall and can be detached easily with the development of embolism. It is recognized that if for any reason the clot in phlebothrombosis does not become detached, a superimposed inflammation of the venous wall may occur, the inflammatory reaction being secondary to the venous clot. Barker and associates believe that this is the usual course of event and there is little or no danger of the clot becoming detached. Whereas this undoubtedly does occur in the exceptional case in which the clot does not become detached, it is hazardous to assume that the occurrence of embolism is not likely in phlebothrombosis. Greenstein has shown conclusively in post-mortem examinations of persons dying from various causes that phlebothrombosis occurs in a high percentage of instances. Of 100 post-mortem examinations, thrombosis of the posterior tibial veins and muscular tributaries was observed in fifty-one and evidence of phlebitis was noted in only four of these. In the remainder there was no evidence of an inflammatory reaction in or around the vein. Also because of the lack of inflammatory reaction of the vein early in the course of phlebothrombosis, there is no arteriolar spasm and for this reason there are few if any symptoms. Because of the ease with which emboli can be detached in spite of absent or minimal symptoms, phlebothrombosis is potentially a fatal lesion. On the other hand, thrombophlebitis, even though the symptoms are severe seldom endangers life although disabling sequelae are likely to persist for months, years, even the remainder of the patient's life.

#### ETIOLOGY

Although venous clotting is more prevalent in certain persons (thrombophiles) injury to body tissues, such as operative obstetrical, or accidental trauma, or destruction of tissue by invasion of neoplastic disease or infection, is the principal predisposing etiologic factor. The precipitating factor is stasis in the venous circulation, which is responsible for the formation of the thrombus in the lower extremities. Circulatory retardation may be generalized as in the elderly patient with arteriosclerotic disease but is maximal in the venous channel of the legs and feet when the patient is confined to bed. On the other hand, phlebothrombosis exceptionally can occur in persons who are not hem-

ridden. McCutchen and Cantey<sup>12</sup> reported five cases of apparently normal persons in whom phlebothrombosis developed even though they were up and about and presumably well. The youngest patient was 48 and the oldest 62 years. Although the increased clotting tendency occurs in the blood of the entire body, it is well known that phlebothrombosis occurs primarily in the vessels of the lower extremity. Investigations of Neumann, Rosol, von Seemen, Hunter and associates,<sup>13</sup> and Greenstein<sup>14</sup> demonstrated that thromboses begin in the veins which drain the calf muscles. Rosol observed thrombosis of the calf vein in 25 per cent of routine post-mortem examination. Hunter, Kivgier, Kennedy and Sneed<sup>15</sup> reported that 6.7 per cent of 361 routine post-mortem examinations disclosed thromboses of the veins of the legs. Greenstein<sup>14</sup> noted thrombosis of the vein of both legs in all his cases. Posterior tibial veins and tributaries to the calf muscles were principally affected. In one instance were the femoral vein involved without concomitant thrombosis of the posterior tibial veins. The greater predilection of thrombosis of the deep veins of the leg is probably due to maximal stasis in those vessels. A patient lying quietly in bed although moving the upper extremities more or less constantly is likely to keep the lower extremities immobile. Since active muscular contraction is a prominent factor in the movement of blood in the veins of the extremities, complete relaxation of the muscles of the lower extremities, particularly those of the calf causes stasis of blood in the veins of these areas. Increased intra-abdominal tension from the use of tight abdominal bandages or gaseous distention of the intestines can compress the vena cava and in cases the venous pressure in the veins of the lower extremity which promote vascular stasis. Another factor favoring venous stasis is hypopnea. Venous circulation is improved by negative intrathoracic pressure and if respiration becomes shallow as the result of an operative procedure particularly laparotomy the aspirating effect of negative pressure is reduced.

#### CLINICAL MANIFESTATION

The clinical manifestation of thrombophlebitis and phlebothrombosis varies considerably. Because of the inflammatory process involving the venous wall the symptoms in thrombophlebitis are severe. We have demonstrated both experimentally and clinically<sup>16</sup> that although the inflammatory lesion is in the vein and this is particularly true when the femoro-popliteal vein is involved the symptoms are the result of spasm of the collateral arterioles because impulses originating in the involved vein are carried by the sympathetic nervous system to the arterioles. Symptoms of thrombophlebitis are fever, pain, edema, redness and swelling of the extremity. The fever is doubtless the result of the inflammatory process involving the venous wall. The other manifestations are the result of ischemia caused by arteriole spasm. Until relatively recently the significance of the redness and coldness of the extremity in phlegmasia alba dolens was not appreciated. That these two manifestations are the result of vasoconstriction can be demonstrated easily by the disappearance following vasodilation. The symptoms and signs in thrombophlebitis, if the condition is not adequately treated are likely to persist with the

production of disabling sequelae such as persistent postphlebitic edema, postphlebitic ulceration, postphlebitic varicosities, and recurrent erysipeloid infections. In the relatively rare case of suppurative thrombophlebitis which occurs in the pelvic veins following criminal abortion, the symptoms are alarming and consist principally of chills and fever. The patient is critically ill and is apt to die unless adequate therapy is instituted promptly. Because of suppuration the intravenous clot becomes liquefied and detached with the production of septic emboli resulting in infarction in the lung and even septicemia. Suppurative thrombophlebitis can occur in other parts of the body as well.

In contrast to the severe clinical manifestations associated with thrombophlebitis, phlebothrombosis is accompanied by few or no manifestations. There may be slight elevation of temperature in a patient who is otherwise progressing satisfactorily; this has been described by Lautre<sup>21</sup> as the little kick. Even more important than transient elevation of temperature is elevation of the pulse rate, which is usually out of proportion to any elevation of temperature. This has been described as the step-ladder pulse. Occasionally the patient complains of apprehension which is unexplainable, and he may have a sense of impending disaster. With few exceptions the erythrocytic sedimentation rate is increased.

#### DIAGNOSIS

Although the diagnosis of thrombophlebitis is not difficult to make because the patient has severe symptoms and usually complains bitterly, the diagnosis of phlebothrombosis is usually made only by careful examination of the patient. It is a rule on our service to examine carefully the calves and feet of all patients past 40 years of age who have had a vascular injury and who are confined to bed. In this way it is possible to detect phlebothrombosis before symptoms appear. Compression of the calf or foot in phlebothrombosis is painful and upon forceful dorsal flexion of the foot pain in the calf and popliteal area is produced (Homan's sign).

Moses<sup>22</sup> has described a sign which he believes is more reliable than others in making a diagnosis of phlebothrombosis. In order to distinguish inflammatory lesions of the skin and subcutaneous lesions of the back of the leg from phlebothrombosis, he suggests that after the presence of tenderness has been determined by applying pressure anteriorly against the calf, pressure be exerted from side to side. If this causes no pain, the lesion may be diagnosed as phlebothrombosis, provided peripheral neuritis has been excluded by careful neurologic examination.

#### PROGNOSIS

As has already been emphasized, the prognosis in the two types of venous thrombosis also differs. Although the patient with thrombophlebitis has severe symptoms, is extremely uncomfortable and is likely to have persistent disabling sequelae unless adequate therapy is instituted relatively early in the course of the disease, there is little or no danger to life with the exception of the unusual case of suppurative thrombophlebitis. On the other hand, the patient with phlebothrombosis who has few or no manifestations and who does not

appear it may have massive pulmonary embolism resulting fatally. It is because of this latter possibility that a fatal outcome in the patient with phlebotrombosis is a potentiality.

# TREATMENT

The treatment of phlebotrombosis is primarily prophylactic. Atraumatic surgical technique should be employed as much as possible in order to produce minimal tissue damage. The use of sharp dissection, the avoidance of massive ligation, and the employment of fine nonabsorbable suture material such as cotton are desirable. By decreasing the amount of tissue damage the clotting tendency is minimized. On the other hand, in any patient who has had any tissue damage as a result of trauma or because of invasion by neoplastic disease or infection, it is imperative to prevent those factors which produce circulatory stasis and measures should be instituted to accelerate the return flow of blood from the lower extremities. This is particularly true in older person with cardiovascular disease for whom bed rest is necessary. Active mobilization of the lower extremities by forcefully contracting the muscles against resistance especially those of the calf, deep breathing and increasing the flow of blood through the arterioles by the application of heat to the body will minimize stasis in the veins of the lower extremities. The application of compression bandages to the lower extremity to obliterate superficial veins will accelerate the blood flow through the deep veins. Early ambulation, which implies not only permitting the patient to get out of bed but also to walk, decreases venous stasis.

If the patient gives a history of having had previous thrombosis, the use of anticoagulants is probably justified. In fact, it is our belief that the principal indication for their use is as a prophylactic measure in patients with a clotting tendency. Reich, Yahr and Eggers<sup>22</sup> advocated the prophylactic use of dicumarol postoperatively. Bauer<sup>23</sup> did not recommend giving heparin before there is evidence of thrombosis. Dennis<sup>24</sup> has used dicumarol prophylactically in the surgical treatment of ulcerative colitis of twenty patients subjected to operation, only three did not receive dicumarol preoperatively and all three died of pulmonary embolism. Bancroft<sup>25</sup> recommended the use of sodium thiosulfate 10 cc of a 10 per cent solution intravenously for three days preoperatively because the antithrombotic effect of heparin is dependent upon its sulfur content.

The curative treatment of thrombophlebitis consists of vasodilatation secured by anesthetization of the regional sympathetic ganglia with procaine hydrochloride. Since these patients are usually too sick to be placed in the prone position the injection is generally done in the lateral decubitus position. The technique of injection is not difficult. Points two fingerbreadths lateral to the spinous processes of the first, second, third, and fourth lumbar vertebrae are chosen. A cutaneous wheal is made at each of these points with a long fine lumbar puncture needle (20 gauge 13.5 to 15 cm in length). The needle is introduced perpendicularly to the skin until it strikes against the transverse process. This latter structure serves as a landmark because whereas there may be considerable difference in the thickness of the subcutaneous fat and the sacrospinal muscle of a large obese muscular man and a little thin woman there is not much difference in the thickness of the bodies of their vertebrae.

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After the transverse process has been identified the direction of the needle is changed slightly either above or below and the needle is introduced for an additional two fingerbreadths. The point of the needle then lies in the retroperitoneal space on the anterolateral surface of the body of the vertebra where the lumbar sympathetic chain is located. Through each one of the four ports, 5 cc of 1 per cent solution of procaine hydrochloride is injected, so that the area in which the sympathetic nerves are located is flooded. This procedure is repeated daily as long as the patient has fever because although the pharmacologic effect of procaine hydrochloride lasts only two hours, the physiologic effect of anaesthetization of the sympathetic ganglia is considerably longer than this.

Almost immediately following the injection there is complete relief of pain, the extremity becomes warm and loses its white discoloration, the temperature rapidly drops to normal and the swelling begins to subside. With few exceptions the patient is well and able to be up within a week or ten days. In the patient with suppurative thrombophlebitis, it is imperative that radical therapy be used early in order to prevent detachment of the infected emboli with production of septic infarction of the lung and possibly septicemia. In order to accomplish this the vein proximal to the site of involvement is ligated and the involved vein is extirpated. If the pelvic veins draining the uterus are involved, ligation of the external iliac just above the bifurcation with simultaneous ligation of the two ovarian veins is the only rational procedure. Whereas previously the prognosis of thrombophlebitis was grave, the immediate institution of radical therapy before fatal septicemia has developed now provides extremely satisfactory results.

The treatment of phlebothrombosis is also rational. Although the symptoms are minimal or absent, a fatal outcome in these patients is a potentiality. Because the thrombus is not attached to the venous wall, it is imperative that either thrombectomy be done or the vein be ligated above the site of the thrombus. It is our belief that this procedure should take precedence over every other operative procedure except measures to combat massive hemorrhage. Ligation is accomplished with the patient in the high-dup position in order to increase the venous pressure in the lower extremity and decrease the possibility of detachment of the clot during the operation. Under local anesthesia a longitudinal incision is made over the femoral vein. The femoral artery is retracted and the vein exposed. Ligatures are loosely placed around the profunda saphenous, and femoral vein above and below the profunda but they are not tied. A transverse incision is made in the superficial femoral vein distal to the junction of the profunda femoris. If a clot is present in the vein, there will be no free bleeding. A glass suture is introduced proximally and gentle suction manometer used until the clot proximal to the opening of the vein is removed. This is followed by free flow of blood from the vein proximally. After the vein has been ligated below the profunda as much of the clot as possible is lifted and the opening is removed. Since the profunda femoris is seldom involved, only the superficial femoral is ligated and divided. The procedure should be done bilaterally because it has been our experience as well as that of others, that if the lesion has occurred on one side it is likely to occur on the

opposite side Greenstein<sup>11</sup> observed that venous thrombosis was bilateral in every instance in which post mortem examination was performed. Compression bandages are applied to the extremity and the patient is instructed to mobilize the extremity as much as possible. He is gotten out of bed the following day.

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## POSTTHROMBOTIC SYNDROME OF THE LOWER EXTREMITY

### TREATMENT BY INTERRUPTION OF THE SUPERFICIAL FEMORAL VEIN AND LIGATION AND STRIPPING OF THE LONG AND SHORT SAPHENOUS VEINS

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DEEP venous thrombosis of the lower extremity, involving the femoral and iliac veins produces permanent morphologic changes in the limb that affect the physiology of the venous circulation. This abnormal physiopathology results in the gradual development of a characteristic syndrome climaxed usually after several years by a chronic indolent ulceration of the lower leg. The most common thrombotic sequelae of this syndrome are pain, edema, varicose veins, induration of the subcutaneous tissues above the internal malleolus, pigmentation, a chronic dermatitis of the skin of the lower leg and chronic ulceration. They develop usually in this order over a period of four to five years after the thrombosis, but occasionally an ulceration may appear within one or two years and sometimes fifteen or twenty years may elapse before it develops. Homans<sup>1</sup> was the first to differentiate between simple varicose ulcers and the so-called postphlebitic ulcer. Since his report in 1917 numerous methods for the cure of this condition have been described but none is successful in all cases. The various types of ointments and local applications including iontophoresis that have been recommended are too numerous to recount. Needless to say the multiplicity of them indicates the ineffectiveness of all of them. Thompson<sup>2</sup> believed fungus infection of the feet to play an important etiologic role in the chronic ulcerations and advised eradication of mycotic foci. This form of therapy may aid in controlling the dermatitis but rarely if ever produces a permanent cure. The most noteworthy of the non-surgical forms of treatment is the application of the plaster type of boot, first described by Unna<sup>3</sup> in 1896, and the more recent modification utilizing an elastic adhesive bandage first reported by Wright<sup>4</sup> in 1930. This form of therapy frequently heals the ulcer but it does not cure it since it invariably recurs after discontinuance of the support.

Homans<sup>1</sup> in 1917 was the first to propose the radical excision of the ulcer and the surrounding pathologic skin and subcutaneous tissues including the deep fascia with the application immediately of a split-thickness skin graft over the denuded area. Similar procedures, some more extensive than others, have been described by Mayo,<sup>5</sup> Trout,<sup>6</sup> Brown and associates,<sup>7</sup> Pennoyer<sup>8</sup> and Douglas.<sup>9</sup> The purpose of this type of treatment was to excise the diseased tissues in the lower part of the leg rather than to correct the abnormal physiology of the venous circulation in the postthrombotic extremity. A more physiologic

and less disfiguring operation was devised by one of us (R R L)<sup>11</sup> in which the communicating veins between the deep and superficial systems were interrupted and also the saphenous vein in the lower leg were removed. The rationale of this procedure was to remove the main varicosities of the lower leg and at the same time divide the communications between the deep and superficial systems of veins so that the increased pressure in the former would not be transmitted directly to the latter. Lumbar sympathectomy has been utilized in our clinic in a number of cases but unless it is combined with some other form of surgical treatment it has not cured the ulcerations.

The results obtained in a series of patients treated at the Massachusetts General Hospital by a number of these methods are shown in Table I. The ineffectiveness of them in many of the cases is apparent and for that reason a new type of surgical treatment consisting of interruption of the superficial femoral vein and ligation and stripping of the long and short saphenous veins has been developed, the results of which to date appear very encouraging. Buxton and his co-workers<sup>12</sup> in 1944 and Buxton and Collier<sup>13</sup> in 1945 were the first to report interruption of the femoral vein as a method of treating postthrombotic ulcerations. Homans<sup>14</sup> in 1945 and 1946 recommended the interruption of the saphenous and the femoral veins in the postthrombotic extremity which shows marked venous congestion. Much credit should go to him because although his publications were not the first he has insisted for a number of years that the canalized postthrombotic vein is a useless structure and should be interrupted. These reports and the fact that in our clinic interruption of the femoral vein for deep venous thrombosis in over 3000 extremities has seemed to prevent the development of the thrombotic sequelae including ulceration were sufficient stimulus to combine interruption of the superficial femoral vein with the complete removal of the long saphenous and the short saphenous vein also when it is varicose. This form of therapy is directed at improving the physiology of the venous circulation in the postthrombotic extremity rather than attempting to cure the ulcer by local measures. In order that the rationale of this treatment may be better understood a short review of the pathologic physiology in the postthrombotic extremity is given.

TABLE I. RESULTS OF TREATMENT OF POSTTHROMBOTIC ULCERATION BY VARIOUS SURGICAL METHODS. THE MASSACHUSETTS GENERAL HOSPITAL.

METHODS	NO.	HEALING		EXTREMITY ALIVE	PERCENT
		FN	FTT FN		
1 Skin graft alone			0	5	100
1 Veinless alone			0		100
2 Excision of ulcer & primary skin graft	7		22	10	7
4 Ligation and division of saphenous vein	1		50	10	50
3 Lumbar sympathectomy	4		50	4	50
6 Ligation and division of communicating veins in the lower leg	—		53	22	43
Total	41		43	57	33

Blalock<sup>4</sup> has demonstrated that the oxygen content of the venous blood from a limb with varicose veins is not diminished. Holling Beecher and Linton confirmed this observation and also showed the same to be true even in the presence of chronic postthrombotic ulcerations. As a result of these findings it is believed that hypo-oxygenation of the blood is not an etiologic factor in the thrombotic sequelae. There are two significant facts, however, concerning the postthrombotic syndrome that should be emphasized since an understanding of them aid in explaining at least some of the etiologic factors in it. First it is believed that the thrombotic sequelae with the exception of pain and edema do not appear immediately but only after the deep veins have become canalized. Second all postthrombotic ulcerations, unless they are extremely large, can be healed temporarily by placing the patient in bed with the leg elevated slightly above the heart level. In support of the first observation, the operative findings in 84 postthrombotic extremities reported in this article revealed that the femoral vein had become canalized in all instances. An analysis of 33 extremities with ulceration (Fig. 1) reveals that there was a period of from one to twenty nine years after the venous thrombosis before the ulcer appeared. The majority or 62 per cent, developed within ten years, and only 4, or 1.6 per cent, at the end of the first year. There will be those who doubt canalization can take place within one year but it has been observed by one of us (B. R. L.) in a patient who also developed an ulceration within that period. Interruption of the canalized superficial femoral vein in this extremity produced rapid healing and it has remained healed for sixteen months without other therapy. The experimental work of Edward and Edward<sup>5</sup> and Beecher<sup>6</sup> also tended to corroborate this observation. The former has demonstrated that after a vein canalizes following phlebothrombosis the venous valves in it are incompetent. Beecher<sup>6</sup> has demonstrated a sustained high pressure in the saphenous vein with incompetent valves during muscular activity whereas with a normal competent valvular system exercise reduces the venous pressure. A comparable situation, even more so, undoubtedly exists in the postthrombotic extremity in which the valves of the deep and the communicating veins also are incompetent. The pressure in the vein under these conditions is far above the colloid oncotic pressure of the blood, resulting in an increased quantity of lymph formation, as demonstrated by Beecher, Foell, and Krogh. In a normal leg the lymphatics would be sufficiently adequate to drain off this increased amount of tissue fluid but as the result of the previous phlebitis the lymphatics have been damaged so that they do not function normally in the postthrombotic states. Holling Beecher and Linton<sup>10</sup> have correlated the increased edema formation with the high sustained venous pressure seen in these patients. Chronic lymphedema is practically universal in all cases and undoubtedly plays a role in the formation and chronicity of the ulceration.

The induration seen in the tissues of the inner and of the lower leg the direct forerunner of the ulceration, it is believed also is secondary to the increased venous pressure. This condition has been designated by one of us (B. R. L.) as stasis cellulitis. The brown pigmentation of the skin of the lower

leg that ultimately appears is due to capillary hemorrhages secondary also to the increased venous pressure. The most marked changes in the skin and subcutaneous tissues and the most common site of ulcerations are on the inner side of the lower part of the leg just above the internal malleolus. It is believed that this is because the communicating veins in this region become incompetent from dilatation since they pass out through tendons and are not supported by the muscles as are the ones higher in the leg. The varicose veins of the long

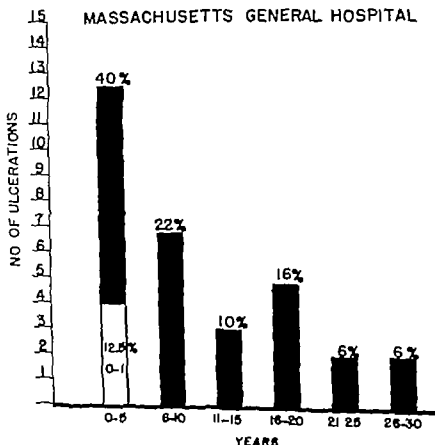


Fig. 1.—Years lived by patients having ulcerations and ulcerations in 3 postthrombotic patients.

and short saphenous veins are most marked on the lower leg below the knee. They gradually develop over a period of years secondary to the increased venous pressure to which they are exposed after the deep veins have been utilized and the communicating veins have become incompetent. The second observation that bed rest with elevation of the extremity below the ulceration is sufficient evidence of these factors is that this treatment is present in practically all diminished and the lymphatics reduced thus reducing the normal

venous and lymphatic circulation. In summary it is therefore believed that the thrombotic sequelae develop as a result of the sustained increased pressure in the veins of the lower extremity and the associated lymphedema.

Experience has revealed that interruption of the femoral vein alone, if ulcerations and ancosities are present, will not suffice to heal the former. These early experiences with poor results from femoral vein interruption alone necessitated the development of an operation which in addition includes the proximal interruption of the long and short saphenous veins, and the stripping of them from the groin and popliteal space respectively to the ankle level. It is believed that the removal of these superficial veins if ulcers overlie them is extremely important, since the ulcerations have persisted in a few cases when the vein was not completely removed.

The selection of the patients for this type of surgical treatment is based primarily on the physical examination rather than on a history of a pre-existing deep venous thrombosis, since such a history cannot be obtained from all the patient. The most important part of the physical examination, to determine the advisability of performing the operation, is to ascertain the competency of the venous valves of the deep communicating and superficial systems of veins. This is done by carrying out the so-called Trendelenburg test. The veins are emptied first of blood by elevating the extremity. A rubber tourniquet is applied to the leg just distal to the knee sufficiently tight to occlude only the superficial vein. The patient then stands up and if the veins below the tourniquet fill within a few seconds it demonstrates incompetent valves of the deep and communicating systems of veins. This observation is sufficient evidence to indicate the desirability of interrupting the superficial femoral vein. Since the dilated superficial veins on the inner side of the lower leg are either the long saphenous vein or its tributaries, removal of the main saphenous trunk from the groin to just below the internal malleolus is indicated also in these extremities. The demonstration of these superficial ancosities in some cases may be difficult due to the extensive fibrosis of the subcutaneous tissues, but chronic skin changes or ulcerations always indicate their presence. Similar conditions on the posterolateral surface of the lower part of the leg and the region of the external malleolus are considered sufficient reason to remove the short saphenous vein. From the experience gained by the study of these cases reported here it is believed that the varicose saphenous veins rarely if ever constitute collateral channels necessary for the return of blood from the extremity.

#### METHOD OF TREATMENT

Many of the patients with the postthrombotic syndrome when first seen require treatment because of chronic ulceration of the lower leg. It is necessary to heal this before operating on the extremity because of the danger of postoperative infection. For this reason when an ulceration is present the treatment is divided into three phases, preoperative, operative and postoperative. If it is healed or an ulcer has not yet developed, of course the first one may be omitted.

*Preoperative.*—The preoperative treatment as a rule is carried out without hospitalization. This is important because the hospital bed is an aid

for more acute cases and in addition the expense to the patient is reduced by a considerable amount. A bland ointment, such as boric acid, is applied to the ulcer. A generous gauze dressing is placed over it. The leg is wrapped with a gauze bandage so that there are several layers of it over the skin from the base of the toes to 3 cm. below the knee. This is covered next with a tight elastic adhesive bandage, making sure to cover the heel completely and extending above the gauze bandage so that the upper portion of the elastic adhesive is applied directly to the skin. This latter point is important, as it keeps the entire dressing in place and prevents it from slipping down. The purpose of the gauze bandage is to prevent maceration of the skin as seen so frequently if the elastic adhesive is applied directly to it over the entire surface of the leg. These dressings are changed weekly at first and later at two-week intervals. As a rule it is possible to heal the ulcer within four to six weeks. After hospital admission a few days are taken to cleanse the skin thoroughly prior to operation. If the ulceration is too large for this type of treatment it has been found advantageous to admit the patient to the hospital. There he is placed in bed with the leg elevated. Mild normal saline or boric acid solution dressings are applied at four-hour intervals. The base of the ulcer develops clean granulations usually within a week under this regime. Then a split-thickness skin graft is applied to the ulcer area. After another period of seven to ten days when the graft has taken sufficiently well the main operation on the veins can be carried out. Penicillin is given during the pre and postoperative periods.

*Operation*—Ether anesthesia has been used routinely. The superficial femoral and the long saphenous veins are exposed through a vertical longitudinal groin incision placed directly over and parallel to the femoral artery pulsations (Fig. 2). The femoral artery and vein are intimately bound together by perivascular scar tissue the result of the previous venous thrombosis. Great care must be taken not to injure the artery in dissecting it free from the vein. It never should be completely isolated and retracted with a rubber tubing, since this may produce arterial thrombosis with gangrene of the lower part of the leg. The superficial femoral vein is isolated for about 3 cm. distal to the profunda femoris branch, which is always carefully visualized to be sure that the common femoral vein has not been isolated. Interruption of the latter and the saphenous vein may produce serious postoperative edema from which the extremity slowly if ever recovers. Venous pressures are taken in the superficial femoral vein by cannulating it with a needle attached to a manometer filled with normal saline solution (Fig. 3). The initial pressure is recorded, a second reading is taken after the superficial femoral vein has been occluded temporarily and finally a third one is taken with both it and the saphenous vein occluded. These pressures are taken as a preoperative measure to ascertain the effect of occluding both of these vessels since occasionally it is found that the pressure rises to an alarming level. A rule has been established that if the pressure rises above 30 cm. after both the veins have been occluded, the stripping is not done until a later date because serious bleeding may occur from the unligated

venous and lymphatic circulation. In summary it is therefore believed that the thrombotic sequelae develop as a result of the sustained increased pressure in the vein of the lower extremity and the associated lymphedema.

Experience has revealed that interruption of the femoral vein alone if ulcerations and varicosities are present, will not suffice to heal the former. These early experiences with poor results from femoral vein interruption alone necessitated the development of an operation, which in addition includes the proximal interruption of the long and short saphenous veins, and the stripping of them from the groin and popliteal space, respectively to the ankle level. It is believed that the removal of these superficial veins if ulcers overlie them is extremely important, since the ulcerations have persisted in a few cases when the vein was not completely removed.

The selection of the patients for this type of surgical treatment is based primarily on the physical examination rather than on a history of a pre-existing deep venous thrombosis, since such a history cannot be obtained from all the patients. The most important part of the physical examination, to determine the advisability of performing the operation, is to ascertain the competency of the venous valves of the deep, communicating and superficial systems of veins. This is done by carrying out the so-called Trendelenburg test. The veins are emptied first of blood by elevating the extremity. A rubber tourniquet is applied to the leg just distal to the knee sufficiently tight to occlude only the superficial veins. The patient then stands up and if the veins below the tourniquet fill within a few seconds it demonstrates incompetent valves of the deep and communicating systems of veins. This observation is sufficient evidence to indicate the desirability of interrupting the superficial femoral vein. Since the dilated superficial veins on the inner side of the lower leg are either the long saphenous vein or its tributaries, removal of the main saphenous trunk from the groin to just below the internal malleolus is indicated also in these extremities. The demonstration of these superficial varicosities in some cases may be difficult due to the extensive fibrosis of the subcutaneous tissues, but chronic skin changes or ulcerations always indicate their presence. Similar conditions on the posterolateral surface of the lower part of the leg and the region of the external malleolus are considered sufficient reason to remove the short saphenous vein. From the experience gained by the study of these cases reported here it is believed that the varicose saphenous vein rarely if ever constitutes collateral channels necessary for the return of blood from the extremity.

#### METHOD OF TREATMENT

Plan. If the patient with the postthrombotic syndrome when first seen is unsuited for treatment because of chronic ulceration of the lower leg it is necessary to heal this before operating on the extremity because of the danger of postoperative infection. For this reason when an ulceration is present the treatment is divided into three phases: preoperative, operative and postoperative. If it is healed or an ulcer has not yet developed, of course the first one may be omitted.

*Pre-operative*.—The preoperative treatment as a rule is carried out without hospitalization. This is important in these days since hospital beds are so

nous vein just below the internal malleolus and pass the stripper upward to complete the removal of the entire trunk. The most important part of the saphenous vein to be removed is that which underlies the ulcer since the poor results in these cases have been in those where the stripping was only carried just proximal to the ulcer area. The incision is carefully sutured without drainage after completion of the stripping. The negligible amount of bleeding from the saphenous tributaries in these cases is always surprising in view of the fact that both the femoral and the saphenous veins have been interrupted. If the short saphenous vein is varicose and if there are chronic skin changes or an ulceration in the region of the lateral malleolus, it should be stripped also from

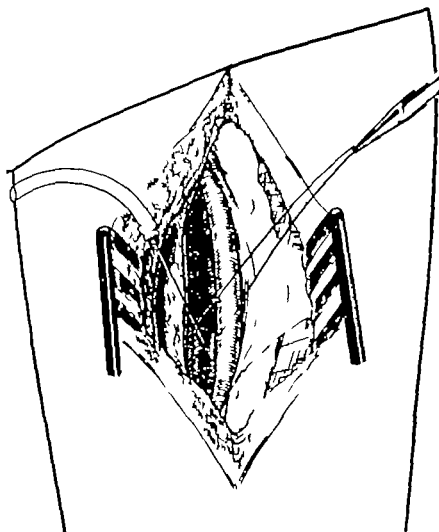


Fig. 1. — Stripping the saphenous vein. The incision is made at the level of the internal malleolus and the vein is stripped upward to the level of the femoral vein. The skin flaps are reflected and the vein is stripped upward to the level of the femoral vein.



saphenous vein in tributaries. More adequate collateral venous channels soon develop with a reduction in the venous pressure so that the stripping may be carried out safely. If a thickened canalized femoral vein is encountered, venous pressures rarely increase more than a few centimeters (Table II) indicating that an excellent venous collateral circulation has already developed. The femoral vein is divided immediately distal to the profunda femoris branch. Each

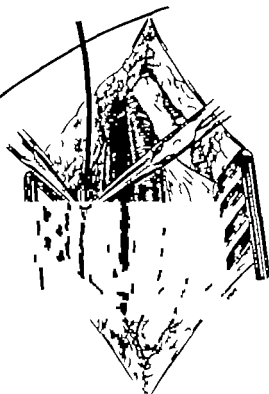


Fig. 4. — Diagram of the surgical approach to the femoral vein. The superficial vein and the saphenous vein are divided into the distal end of

and is ligated with a ligature of silk or cotton. The patient is then placed in Trendelenburg position and the venous pressure in the extremity and the saphenous trunk is stripped from the groin to just below the internal malleolus. After being interrupted at the saphenofemoral junction. An internal type of stripper is used, similar to the one first described by Halbrook (Fig. 4). In some cases it passes readily from the groin to the ankle; in others it may be necessary to hold the saphenous

injection of a sclerosing solution may be necessary to eradicate a large varix that is still present in some instances. A varying degree of lymphedema is often seen and in such cases the patient is instructed to wear an elastic bandage or stocking until this disappears.

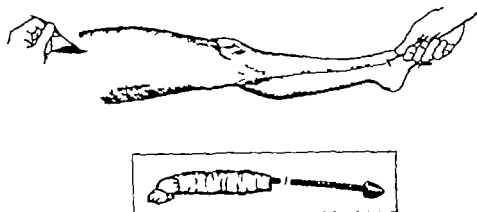


FIG. 4.—An elastic strip, drawn along the leg, gradually strips the varix from the skin. The strip is then drawn over the varix. When it is removed in this manner the varix breaks. If it does another location is frequently necessary. Complete the removal of the varix.

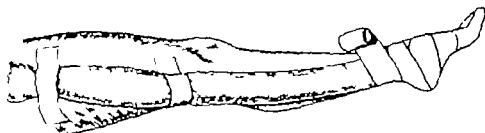


FIG. 5.—An elastic strip, drawn along the leg, gradually strips the varix from the skin. The strip is then drawn over the varix. When it is removed in this manner the varix breaks. If it does another location is frequently necessary. Complete the removal of the varix.

#### DISCUSSION

This report is based on 49 patients who presented thrombotic sequelae in one or both lower extremities. There were 31 or 63 per cent females and 18 or 37 per cent males. The age distribution reveals that 34 or 70 per cent were between 40 and 60 years of age. The youngest was 21 years and the oldest 69 years of age (Table III). The chief complaint of these patients when first seen were chronic indolent ulcer in 25 or 50 per cent, varicose veins in 14 or 30 per cent, swelling of the extremity in 10 or 20 per cent, and phlebitis in 3 or 6 per cent. A definite history of pre-existing deep venous thrombosis of the lower extremities was given by 46, or 94 per cent of the patients and in 3 it was not obtained. It had occurred 1 to 11 years in 23, or 47 per cent of the

TABLE II. A. NOON PRESSURES IN FEMORAL VEIN OF THIRTY POSTOPERATIVE EXTREMITIES, MARINE CH. AFTER GENERAL HOSPITAL

CASE NO.	INITIAL FEMORAL VEIN PRESSURE	AFTER OCCLUSION OF SUPERFICIAL FEMORAL VEIN	AFTER OCCLUSION OF SUPERFICIAL FEMORAL AND LONG SAPHENOUS VEINS
1	3.5	15.0	19.0
2	4.0	6.5	16.5
3	4.0	15.5	16.0
4	4.5	7.0	7.0
5	6.0	8.0	8.5
6	6.0	21.0	21.0
7	6.0	20.0	20.0
8	6.0	15.0	15.5
9	6.0	9.0	10.0
10	7.0	11.0	14.0
11	7.0	23.0	44.0
12	7.0	12.5	16.0
13	7.5	14.5	14.5
14	7.5	12.5	14.5
15	8.0	8.5	8.5
16	8.5	14.5	14.5
17	8.5	0	9.0
18	10.0	12.0	27.0
19	11.0	11.5	15.0
20	11.0	16.5	19.0
21	11.5	12.0	14.0
22	12.5	22.5	45.0
23	12.5	19.5	22.0
24	12.5	14.0	15.0
25	13.5	14.5	12.5
26	14.0	18.0	19.0
27	16.0	17.5	17.5
28	17.0	20.0	24.5
29	20.0	21.9	24.0
30	20.0	20.0	45.0
Lowest	3.5	6.5	5
Highest	20.0	23.5	45.0
Mean	9.5	15.5	19.0

In centimeters of normal saline solution

the popliteal space to a point distal to the lateral malleolus. The patient is turned in the prone position on the operating table in order to facilitate this part of the operation. The vein is isolated through a transverse incision in the popliteal space. An every effort is made to remove the entire trunk. After closure of all the incisions, gauze roll 5 to 6 cm. in diameter is placed over the course of the long saphenous vein (Fig. 5) and the extremity bound from the toes to the groin with two or three inch width elastic bandages.

*Postoperative.*—Penicillin twenty thousand units are administered intramuscularly every three hours for five days. The foot of the bed is elevated on shock blocks for twenty-four hours. The patient is allowed to be ambulant on the first or second postoperative day. The skin sutures are removed on the fifth postoperative day and usually the patient is discharged from the hospital on the seventh to the tenth day with instructions to wear an elastic bandage from the toes to the knee during the day. Regular back-ups are made at two-week intervals at first and then monthly for the first three months. A small

Lymphedema was not only the most common sequel occurring in all the extremities but it had persisted the longest period since it developed concomitant with the venous thrombosis. The other sequelae developed at varying intervals in the postthrombotic period. It is interesting to note that there was a great difference in the time of appearance of the ulcerations in the various patients. They developed within a year in 4 of them, whereas in two

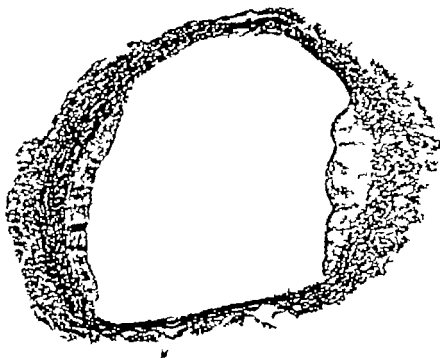


Fig. 1—An enlargement of a radiograph of the thickened and ulcerated postthrombotic femoral vein. Note the absence of the normal lumen.

cases the ulcerations appeared between the first and second years after the onset of the thrombosis. The majority of them (62 per cent) (Fig. 1) appeared within the first year. The ulceration is not always of the great extent that this time of appearance in the fact that less than one-half of the extremities were ulcerated. It is important to note that the ulceration is not always of the great extent.

The surgical treatment performed in 84 patients with extremities complicated by the interruption of the femoral vein just distal to the profunda femoris. The ligation of the long saphenous vein at the saphenofemoral junction and the removal of it from the groin to the ankle is a simple procedure. In addition the short saphenous vein when it was found to be diseased. It is important that the common femoral vein should not be interrupted. See this figure with the saphenous vein interruption which shut off the main flow of the venous return.

TAB III A D AIR AIR FUEL OR P THER WITH POSTHYPEREMIC SYNDROME  
M CHL PTIC O ERAL HOSPITAL

AGE (YE)	M	F	FFM	TOTAL	PER CENT
21 to 30	3	1	3	4	75%
31 to 40	4	3	7	11	
41 to 50	6	15	21	27	
51 to 60	1	9	10	11	
61 to 70	7	1	8	9	
1 to 70	14 (31.4)	11 (25.4)	25	40	100

Turnover 1 year old, 0.5 years

patient and unilaterally in 46 (55 per cent). Physical examination and operative findings revealed a higher incidence of pre-existing deep venous thrombosis than was indicated by the history (Table IV). Postthrombotic changes in the extremities were observed bilaterally in 2, or 71 per cent of the patients and unilaterally in 14, or 90 per cent making a total of 84 (100 per cent) of the extremities. This higher incidence was sufficient to warrant operation since a perivascular postthrombotic matrix and sclerosis of the femoral vein (Fig. 6) were observed in 10 (83 per cent) of the extremities and unilaterally in 14, or 17 per cent making a total of 84 or 100 per cent of the extremities. The pre-existing deep venous thrombosis filled surgical condition in 90 patients, parturition in 16, medical losses in 8. It occurred spontaneously in 1 and in 70 history was bilateral.

TAB	IV	PREFACE	D	A	C	T		NOTES ON POSTHUMOUS A	MORAL
			M	G	A	S	O		HONESTY

LAD CO	INTENT		PER NO AL EKA		TROY		OPAR TIS		TANVON				
	EXTD PER		THERED		EXTREMI		P TI VTI		THER				
	TI	PER	PER	PER	PER	PER	PER	PER	PER	PER			
H lateral rth	20	41	40	64	18	71	70	1	23	71	70	81	
Bilateral rthout	3	6											
Unilateral	26	31	76		24	14	29	14	17	14	29	14	17
Total	49		7		4		24		40		84		

The most common signs and symptoms in the series of the frequency seen in these 84 extremities with the postthrombotic syndrome were: edema in 84 or 100 per cent; pigmentation in 80 or 93 per cent; discoloration in 79 or 94 per cent; pain in 64 or 76 per cent; stasis dermatitis in 49 or 59 per cent; skin cellulitis in 48 or 57 per cent; ulcer in 30 or 36 per cent. Of the little toe I was still painful when the patient was admitted to the hospital. 7 were healed but gave a history of repeated recurrences. The past, and R had been healed before the patient's admission to the hospital with elastic pressure bandages. All except of the pen one were healed with bed rest, elevation of the extremity, moist dressings, and intravenous injections of penicillin, so that the limb was in a satisfactory condition for surgery with seven to ten days. The two unhealed ones were covered with split-thickness skin grafts before proceeding with the operation on the limb.

mean 18.5 cm. With both this vessel and the long saphenous vein occluded the lowest pressure was 9.5 cm, the highest 45 cm, and the mean 19 cm. The readings obtained in 30 of the extremities are shown in Table II. An analysis of these proves that in the majority of postthrombotic extremities neither the superficial femoral nor the long saphenous vein or both of them, is necessary for the return of blood from the limb. The second reason for determining the level of venous pressure in the extremity was in the event that it became so elevated that severe hemorrhage might occur following the tripping of the saphenous vein. The pressure in 4 instances with both vessels occluded rose to approximately 45 cm. In the first two there were no complications following the procedure but extensive postoperative ecchymoses occurred in the third one, so that in the fourth case the tripping was postponed for one week when the pressure had dropped to 4 cm, a more nearly normal level.

The postoperative complications were few and not serious (Table VI). The most troublesome one was edema in 6 extremities, necessitating the use of an elastic support. The mortality rate was zero. At the present time it is our opinion that no extremity has been made worse by the operative procedure as described.

TABLE VI Incidence of Complications in Extremities, Postthrombotic Extremities, Mary Cheney General Hospital

COMPLICATIONS	NUMBER
Sepsis in groin incision	1
Hemostoma in groin incision	1
Lymph collection in groin incision	1
Penicillin Dermatitis	
Secondary aneurysm	1
Edema of extremity	6
Mortality rate	0

A number of the patients with persistent ulcerations had previous surgical procedures without benefit. These included 14 instances of interruption of the saphenous vein at the saphenofemoral junction with and without injection of sclerosing solution, 1 with multiple ligation of the long saphenous vein, 3 lumbar sympathectomies, and 3 patients who had had interruption of the superficial femoral veins. The poor results obtained with these forms of therapy are not surprising in view of our past experiences (Table I). The fact that 3 did not do well after superficial femoral interruption alone over periods of twenty-four, fifteen and twelve months is considered to be of significance in determining the necessity of combining it with ligation and stripping of the saphenous veins. As a secondary procedure this has been carried out in these three cases with gratifying results that for periods of two, eight, and eight months.

The follow-up statistics on the 84 postthrombotic extremities over a period varying from one to sixteen months (Table VII). An analysis of the results revealed that pain was a symptom in 54 or 64 per cent of the extremities. It was relieved in 34 or 63 per cent and incompletely relieved in 20 or 37 per

The rationale of this method of treatment it is believed, is that the venous blood is shunted into smaller deep veins which still have competent valves, thus possibly reducing the venous pressure especially during exercise; it prevents a direct reversal of the venous blood flow down the deep veins from the large venous reservoirs of the trunk when the erect position is assumed; it preserves the profunda femoris, the medial and the lateral circumflex femoral veins as collateral channels for the return of the blood from the extremity and it removes the main superficial varicosities.

Bilateral superficial femoral vein interruption and ligation with stripping of the long saphenous vein were performed on 35 or 71 per cent. of the patient. 14 had it done only on one leg (Table V). Four of the patients had the stripping done as secondary procedures, 3 because of the recurrence of the

TABLE V. OPERATIVE PLAN SURF: FIFTY FIVE PATIENTS WITH POSTPHLEBITIC  
H. B. M. MASSACHUSETTS GENERAL HOSPITAL

OPERATION	PATIENTS NO. PER CENT.		EXTREMITIES NO. PER CENT.	
	NO.	PER CENT.	NO.	PER CENT.
	25	71	70	57
	14	29	14	17
	9	20	9	18
	6		6	
			2	

Ligation & stripping of short saphenous vein  
Flap graft to heel

ulceration after femoral vein interruption alone and the fourth because the femoral vein pressure rose to a level of 45 cm. after interruption, so the stripping was delayed for a week until the pressure had fallen to 24 cm. In the latter case it was feared that serious hemorrhage might occur from the tributaries of the saphenous vein with such high venous pressure. Combining all these operative procedures there was a total of 84 extremities that had both the superficial femoral vein interrupted and the long saphenous vein ligated and stripped. The short saphenous vein was interrupted at the saphenopopliteal junction in 9 extremities and in addition stripped in 6 others. This made a total of 15 extremities in which this vein was interrupted. One patient who had recurrent ulcer over the lateral malleolus showed an enlarged incompetent short saphenous vein which should have been removed as it is believed the persistence of this vessel explained the recurrence of the ulceration.

Venous pressures were taken during the operation for two reasons in the superficial femoral vein before and after interrupting it and again with the long saphenous vein also occluded. First these readings were taken to determine if either one or both of the vessels, especially the saphenous, were important collateral channels for the return of blood from the limb. The initial pressure varied considerably. The lowest was 3.5 cm. of normal saline solution and the highest was 20 cm.; the mean also was 9.5 centimeters. After occluding the superficial femoral vein the lowest value was 6.5 cm. the highest 22.5 cm. and the

mean 13.5 cm. With both this vessel and the long saphenous vein occluded the lowest pressure was 9.5 cm, the highest 45 cm, and the mean 19 cm. The readings obtained in 30 of the extremities are shown in Table II. An analysis of these proves that in the majority of postthrombotic extremities neither the superficial femoral nor the long saphenous vein or both of them, is necessary for the return of blood from the limb. The second reason for determining the level of venous pressure in the extremity was in the event that it became so elevated that severe hemorrhage might occur following the stripping of the saphenous vein. The pressure in 4 instances with both vessels occluded rose to approximately 45 cm. In the first two there were no complications following the procedure but extensive postoperative ecchymoses occurred in the third one, so that in the fourth case the stripping was postponed for one week when the pressure had dropped to 41 cm, a more nearly normal level.

The postoperative complications were few and not serious (Table VI). The most troublesome one was edema in 6 extremities, necessitating the use of an elastic support. The mortality rate was zero. At the present time it is our opinion that an extremity has been made worse by the percutaneous procedure as described.

TABLE VI. POSTOPERATIVE COMPLICATIONS IN EIGHTY-ONE POSTTHROMBOTIC EXTREMITIES, MAY, ONEHUNDRED FORTY-ONE, HOSPITAL

COMPLICATION	NUMBER
Wepers in groin incision	1
Hematomas in groin incision	3
Large collections in groin incision	1
Periculis Dermatitis	
Secondary aneurysm	1
Edema of extremity	6
Mortality rate	0

A number of the patient with persistent ulcerations had previous surgical procedures without benefit. These included 14 instances of interruption of the saphenous vein at the saphenofemoral junction with and without injection of sclerosing solutions, 1 with multiple ligations of the long saphenous vein, 3 lumbar sympathectomies, and 3 patient who had had interruption of the superficial femoral vein. The poor results obtained with these forms of therapy are not surprising in view of our past experience (Table I). The fact that 3 did not do well after superficial femoral vein interruption alone over period of two, two, fifteen, and twelve months I considered to be of significance, indicating the necessity of establishing it with ligation and stripping of the saphenous veins. A secondary procedure thus has been carried out in these three cases with gratifying result to date for period of two, eight and eight months.

The follow-up statistics on the 84 postthrombotic extremities cover a period varying from one to sixteen months (Table VII). An analysis of the results revealed that pain was relieved in 34 or 61 per cent and incompletely relieved in 20 or 37 per



The rationale of this method of treatment it is believed, is that the venous blood is shunted into smaller deep vein which still have competent valves, thus possibly reducing the venous pressure especially during exercise; it prevents a direct reversal of the venous blood flow down the deep veins from the large venous reservoirs of the trunk when the erect position is assumed; it preserves the profunda femoris, the medial and the lateral circumflex femoral veins as collateral channels for the return of the blood from the extremity; and it removes the main superficial varicosities.

Bilateral superficial femoral vein interruption and ligation with stripping of the long saphenous vein were performed on 75 or 71 per cent, of the patients. 14 had it done only on one leg (Table V). Four of the patients had the stripping done as secondary procedures, 3 because of the recurrence of the

TABLE V. OPERATIVE PROCEDURES. FORTY-NINE PATIENTS WITH POSTERIOR VENOTROMBOSIS. MAYO CLINIC, GENE RAL HOSPITAL

OPERATION	PATIENTS PER CENT		EXTREMITIES PER CENT	
	NO.	PER CENT	NO.	PER CENT
1	35	71	78	87
	14	29	14	17
	9	20	9	19
Ligation & stripping of short saphenous vein	0		0	
Skin graft to ulcer	3		2	

ulceration after femoral vein interruption alone and the fourth because the femoral vein pressure rose to a level of 45 cm. after interruption, so the stripping was delayed for a week until the pressure had fallen to 4 cm. In the latter case it was feared that serious hemorrhage might occur from the tributaries of the saphenous vein with such a high venous pressure. Combining all these operative procedures there was a total of 84 extremities that had both the superficial femoral vein interrupted and the long saphenous vein ligated and stripped. The short saphenous vein was interrupted at the saphenopopliteal junction in 9 extremities and in addition stripped 6 there. This made a total of 15 extremities in which this vein was interrupted. One patient who had a recurrent ulcer over the lateral malleolus showed an enlarged incompetent short saphenous vein which should have been removed, as it is believed the persistence of this vessel explained the recurrence of the ulceration.

Venous pressures were taken during the operation for two reasons: in the superficial femoral vein before and after interrupting it and again with the long saphenous vein also occluded. First these readings were taken to determine if either one or both of the vessels, especially the saphenous, were important collateral channels for the return of blood from the limb. The distal pressure varied considerably. The lowest was 33 cm. of normal saline solution and the highest was 90 cm. the mean value was 95 centimeters. After occluding the superficial femoral vein the lowest value was 65 cm. the highest 72.5 cm. and the

was only 3 ears. Another fact in favor of the unhealed ulcers, it is believed was the fact that the saphenous vein were not removed from beneath the ulcer areas. It will appear however from these statistics that the earlier adequate surgical treatment is performed in the ulcer group the better is the chance of cure. It is realized, of course that the follow-up period in the cases reported here is too short to claim permanent cure by this method of a chronic condition which has baffled the medical profession for centuries, but nevertheless the results to date are sufficiently encouraging to warrant further trial.

#### CONCLUSIONS

1 Deep non thrombotic of the lower extremity involving the femoral and the veins produce permanent morphologic changes in the extremity that result in a characteristic postthrombotic syndrome.

The postthrombotic syndrome is characterized by the following states which appear usually in the edema, varicose veins, stasis cellulitis, stasis dermatitis, pigmentation and finally ulceration.

3 It is believed that the postthrombotic syndrome develops primarily as a result of a high sustained venous pressure in the extremity due to incompetent valves in the deep communicating and superficial systems of veins following amputation of the deep veins.

4 Interruption of the femoral vein distal to the profunda femoris branch ligation and stripping of the long saphenous vein, and in addition the short saphenous vein if it is diseased has been performed on 84 extremities presenting the postthrombotic syndrome in various stages. The common femoral vein should not be interrupted and the importance of removing the entire main saphenous trunk is emphasized.

5 None of the extremities has been injured by this procedure indicating that the superficial femoral and the saphenous veins are not necessary collateral venous channels in the postthrombotic extremity.

6 The postoperative complications have been few and not serious, and the mortality rate was zero.

7 The results of a follow-up interval varying from one to sixteen months in 84 extremities subjected to this form of treatment are encouraging but further ears of observation are necessary to determine the true value of this method.

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TABLE VII FOLLOW-UP EXAMINATIONS OF THE LIMBS IN EXHIBIT FOR POST-OPERATIVE EXTREMITIES, M. WITH (GENERAL HOSPITAL)

SQUAM	LIMB I		LIMB II		STILL PRESENT IN PER CENT	
	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT
Pain	31	61	31	61	25	27
Edema	84	100	28	45	46	85
Varicose veins	79	94	26	37	81	87
Healed ulcers	4	37	18	37	20	87
Healed dermatitis	4	34	16	33	13	87
Pigmentation	80	5	0	0	80	100
Ulceration	26	47	29	50	7	201

Relieved with post-operative injections of sclerosing solution.

One practically healed though somewhat postoperatively. 2 occurred, healing with injections. 2 occurred, and the lower 2 are present but not healing.

cent. Edema was present in II and was relieved in 38.4 per cent, so that no elastic support had to be worn whereas in 46 or 33 per cent it was not completely relieved necessitating the wearing of an elastic bandage or stocking. Many of these patients are improved and it is felt will ultimately be able to go without support. Some patients have worn such protection for so long that it is difficult to get them to discard it. Varicose veins were demonstrable in 79 or 84 per cent of the extremities. They disappeared after the operation in 6 or 33 per cent and with a few injections of a sclerosing solution in the remaining 7, or 67 per cent of the extremities have been relieved. Induration of the subcutaneous tissues remained in 48 or 57 per cent. It was relieved in 18, or 37 per cent and is still present but improved in the remaining 30 or 63 per cent. It is less often observed in 49 or 38 per cent, was relieved in 16 or 3 per cent and is still present in 13, or 27 per cent. Pigmentation of the skin of the lower leg was the last affected of the thrombotic sequel. It was observed in 80 or 9 per cent and is still present in 11 of these extremities. There has been slight improvement in the intensity of it seems to have diminished somewhat but it is felt that it will never entirely disappear. It is the least troublesome of the sequelae from the patient's viewpoint. It has been present in 36 or 43 per cent of the limbs. The ulcers healed in 20 or 60 per cent. 17 or 20 per cent have not healed. In the latter group one who at all healed after 3 months, had recurred and was temporarily healed with injections of sclerosing solutions in the same area. In the latter group the ulcers recurred and have not yet healed.

The plan for the treatment of these 7 ulcers is not entirely clear but the future of the limbs before the treatment was carried out may be a fair index. Most of the legs in the group show a greater degree of local fault in the tissues beneath and around them for fibrosis is usually found than in those of shorter duration. The mean age of the unhealed group of 7 is 9 years whereas in the healed group of 20 it was 5 years. If four patients from the latter re-ulcerated while the duration of the ulcers was fifteen, sixteen, twenty-four and thirty years respectively, 33 whom the mean age

# THE SURGICAL TREATMENT OF ESSENTIAL HYPERTENSION

## IV CASE SELECTION AND TECHNIQUE AS INFLUENCING RESULTS

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**T**HOUSANDS of operations have been performed to date for hypertension but neither the classification and case selection nor the technique employed has been uniform. It is, therefore, difficult to compare the results of various clinics engaged in this work. In this communication we wish to present our classification, case selection, and the techniques employed and their influence on results. This topic is obviously controversial and leaves room for a great deal of discussion.

### CLASSIFICATION OF ESSENTIAL HYPERTENSION

The basis of all classifications is the concept of Keith, Wagener and Barker that hypertension per se causes increasing damage in cerebral, retinal, cardiac and renal structures and that the stage of the disease can be defined by the advancing damage in these organs. In a previous report de Takats, Heyer and Keeton presented a table which was based on the combined data of Wagener and Keith, Palmer and Smithwick, and our own earlier experiences. As a weakness of all attempts at grading hypertension one point became obvious: the degree of involvement in the brain, retina, heart, kidney or peripheral vessels does not run a parallel course and a patient with a severe cerebrovascular accident can have surprisingly intact cardiac and renal function. For this reason, subsequent workers have used subdivisions of this classification. Peet and Isberg<sup>1</sup> used six groups. While the first and sixth groups are identical with Wagener and Keith's first and last (fourth) groups, they introduce a group of patient with early hypertension in whom symptoms predominate but who display no organic involvement except in the fundi, and another three groups in which cardiac, cerebrovascular or renal disease are predominant. Smithwick<sup>2</sup> in his latest communication used twelve groups, determined by sex, age and pulse pressure. Hinton and Lord graded the severity of hypertension on the basis of four in each of the organs: brain, retina, heart, and kidney. A total count of more than eleven contraindicates operation.

Our group uses a simple classification in the three groups, which are essentially those of Wagener and Keith except that Group 1 is a combination of I and early II of Wagener and Keith and Group 3 is a combination of late grade III and IV of Keith and associated. This classification arose out of our experience that the malignant and premalignant phases of hypertension are not a surgical problem and second, that the grade I and early grade II hypertensives

<sup>1</sup>Presented at the annual meeting of the Society for Vascular Surgery, Atlantic City, N. J., June 8, 1947.

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Splanchnic nerve section as practiced today varies in extent and we shall deal with these variations later. It can diminish sympathetic-adrenal activity, inhibit reflex renal spasm, and diminish general arteriolar tone. How much benefit occurs from inhibition of afferent impulses from the viscera is not sufficiently known, but the hypothalamus is readily activated from many outside stimuli. Certainly it does not affect the psyche, the parenchymal lesion in the kidney and probably not the adrenal cortex, although some of our early work did suggest that lipid storage occurred there after splanchnic section.<sup>12</sup> Little is known about the late effects of splanchnic section on the adrenal cortex. From the standpoint of case selection, then, it is important not only to exclude patients with excessive vascular damage as manifested in the premalignant and malignant phase of hypertension, but also those in whom psychic, cortico-adrenal, or renal parenchymal factors are predominant.

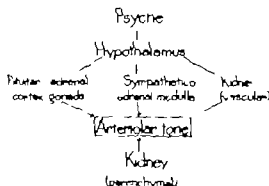


Fig. 1.—The main

Sympathectomy may interrupt the tract between system. It may diminish the adrenal supply from the kidneys, it should not decrease the arterial tone. Whether the cortico-adrenal lipids in the kidneys are affected by splanchnic nerve section is unknown.

#### CONTRAINDICATIONS TO OPERATION

These considerations, then, make our contraindications clear. The contraindications to splanchnic nerve section for essential hypertension can be summarized under four headings:

- 1 Extensive organic damage to brain, retina, heart, or kidney
- 2 Mechanical obstruction to circulation
- 3 Marked psychic involvement
- 4 Obvious pituitary-cortico-adrenal activity

1. Extensive organic damage to brain, retina, heart, or kidney. For us, persistent papilledema and nitrogenous retention are absolute contraindications. If

there is no indication of the circulation, such as exists in aortic regurgitation, correlation of the aorta, but also in the rigid, sclerotic aorta of all arteriosclerotic patients with a high pulse pressure and a diastolic pressure stable

of Wagoner and Keith can be grouped together since result of operation in this group are uniformly excellent. Accordingly the three groups of essential hypertension are:

Group 1. Age below 40 years, minimal or no detectible organic damage, normal blood pressure on complete rest or in laboratory, casual diastolic pressures less than 100 mm Hg.

Group 2. Age from 40 to 55, are moderate vascular sclerosis in all organs, all demonstrable organ-system diastolic pressure cannot be lowered below 110 mm Hg by any method, rising diastolic pressure during the course of first 6 months.

Group 3. All age recurrent retinal hemorrhages and exudates or papilledema, high fixed diastolic pressure, blood cannot be lowered below 120 mm Hg, congestive or apical heart failure, poor renal function, necrosis cerebri, stroke accidents, renal malignant or premalignant, all of hypertension, its root cause is a maladjustment, usually in the nervous or depressive system.

All these classification are simply the expressions of the degree of organic vascular damage. Another viewpoint namely whether the hypertension is renal or nonrenal does not find any precision in these gradings. Some authors feel that the neurogenic hypertension is the ideal case for sympathectomy whereas the renal group should be excluded from the operation. Two of us, in an article published recently, came to the paradoxical conclusion that the renal group did better than the so-called neurogenic especially since the neurogenic group turn out to be more and more a neuroendocrine state.

What is urgently needed is separation of the renal from the nonrenal factor. It is becoming obvious that both may operate in the same patient in varying sequence and varying proportion. Thus, a existing neurogenic mechanism may produce repeated cortical ischemia in the kidney and if the terminating experiments of Trueta and his co-workers. Conversely a renal hypertension produced experimentally may enter a second neurogenic phase indicated by Ogden and his group.<sup>14</sup> For practical purposes, neither the blood pressure itself nor that of the barbiturates has given a lead-out answer. The use of monoethyl ammonium chloride (etimon) a sympathetic depressant produces rapid fall in blood pressure in an animal with a Goldblatt clamp and also in one with the moderator nerve sectioned.

To complete the picture further the pituitary-cortico-adrenal mechanism has to be taken into consideration not only in the typical Cushing's syndrome but in many patients with hypertension in whom neurogenic factor is dominant and whose general adaptive mechanism is stimulated.

The emotional element the personality of the patient with hypertension, has been the subject of extensive studies and suffice it to say here that while treatment directed toward this factor has never been capable of definitely lowering blood pressure, the severity of the psychoneurotic element may contraindicate operation. In such patients, psychotherapy should precede and not follow surgical treatment, as born out by some unfortunate personal experiences.

Looking at hypertension then from the standpoint of the surgeon, it must become clear to him that in the complex mechanism of hypertension he can influence some of the factors. The so-called redeployment in the diagram (Fig. 1).

the first lumbar segment and often the second. He too has done high l resectomy of late. Hinton advocated a transpleural approach through the tenth rib and he removes the splanchnic nerve from the fifth dorsal segment to the celiac ganglion the chain from the third dorsal to the third lumbar segment. Grimson,<sup>22</sup> in his total sympathectomy removed the entire splanchnic nerve and the sympathetic chain from the stellate ganglion to the fourth lumbar segment in two, three and four stages.

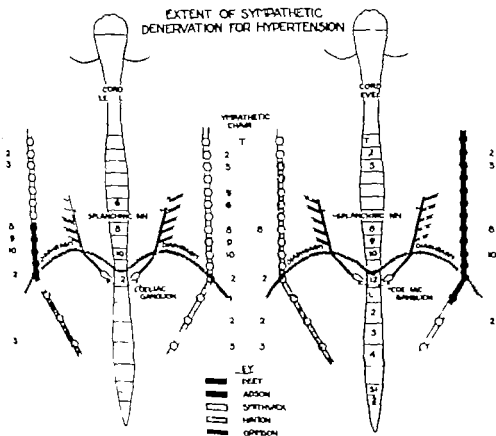


Fig. 1.—Extent for sympathetic denervation for hypertension. The approaches of Dees and Takats which are extrapleural, those of Hinton and Grimson are transpleural. Our recent papers described an extrapleural approach in the vast majority of cases but by this on this but based on very personal experience these figures are shown.

Obviously the mortality must rise with the extent of the operation and the acceptance of malignant or premalignant types of hypertension for operation.

Since 1940 we adopted the technique of Smithwick and most of our present operations are based on his procedure except that the twelfth rib is not resected but the eleventh is in its entirety and that the two adjacent ribs are approximated with finail or wire or No. 1 chrome suture. The removal of the major splanchnic nerve from the mid-thoracic level to the tip of the celiac ganglion



lived between 100 and 110 mm. of mercury. Arteriolar tone in these patients is not significantly increased.

3. Marked psychic involvement. Neither blood pressure nor mental attitude is improved after operation and surgery often aggravates the mental status in such patients.

4. Obvious pituitary-corticoadrenal activity which in our present state of knowledge may be influenced only by radiation or possibly by a low sodium diet but not by surgery. This may be measured by any of the tests used for the detection of corticoadrenal insufficiency except that deviation from the normal is on the side of hyperfunction. This group is often labeled neurogenic but neurohormonal or neuroendocrine is more appropriate. Recently through the work of Selye, and Sayers and his associates, it has become well established that under various types of stress, corticoadrenal cholesterol is emptied. The latter authors showed that according to the intensity and duration of pituitary stimulation and the time after which the adrenal gland is examined, five degrees of adrenal response may be recognized. In applying such experimental data to the subject of human hypertension, further studies are now in progress, which need not be discussed here. Suffice it to say however that corticoadrenal activity seems to be present in many forms of human hypertension, and that this angle of the problem has been so far neglected, compared with the renal factor. It is to be stressed here that we are not discussing the full blown picture of the Cushing syndrome but a secondary corticoadrenal stimulation accompanying many forms of essential hypertension. I would predict that the emphasis which is on the renal factor today will shift in the next few years to the corticoadrenal factor.

#### VARIATIONS IN TECHNIQUE

There are many variations, extensions, and reductions in the extent of sympathetic denervation, but they may be crystallized around five basic patterns which are presented in the accompanying diagram. Our apologies are due those who have used other modifications, but for the sake of simplifying the discussion, these five techniques have been depicted (Fig. 2). To carry this diagram up to date, we are relying on recent personal communications.

The technique of Adson and Craig removes through a retroperitoneal subdiaphragmatic exposure the major splanchnic nerve from the diaphragm to and including the tip of the celiac ganglion, together with the two upper lumbar ganglia. The last available report of Adson and Allen on results obtained with this technique was made in 1940.<sup>17</sup> Craig, in a personal communication, stated that he is now extending this operation to various supradiaphragmatic level. The technique of Peet<sup>18</sup> which according to his latest personal communication is still the original supradiaphragmatic retropleural approach, done in one stage, removes the splanchnic nerve from the eighth dorsal segment to the diaphragm and the chain from the eighth to the twelfth dorsal segment, inclusive. Smithwick<sup>19</sup> combined the two approaches by a transdiaphragmatic route and removes the splanchnic nerve from the eighth dorsal segment to the celiac ganglion and the chain from the eighth dorsal segment to at least include

the first lumbar segment and often the second. He too has done high loral sympathectomies of late. Hinton advocated a transpleural approach through the tenth rib and he removes the splanchnic nerve from the fifth dorsal segment to the celiac ganglion, the chain from the third dorsal to the third lumbar segment. Grimsom,<sup>22</sup> in his total sympathectomy removed the entire splanchnic nerve and the sympathetic chain from the stellate ganglion to the fourth lumbar segment in two, three and four stages.

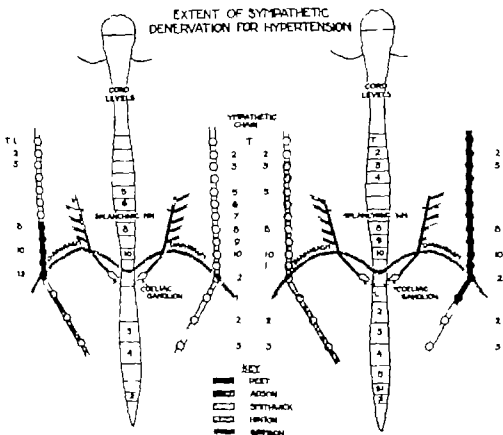


Fig. 2.—Extent for sympathetic denervation for hypertension. The approaches of Post and Smithwick are extrapleural; those of Hinton and Grimsom are transpleural. Quite recently Postre described an extrapleural approach with the extent of denervation used by Hinton. Drawing based on recent personal communication from these authors.

Obviously the mortality must rise with the extent of the operation and the acceptance of malignant or premalignant types of hypertension for operation.

Since 1940 we adopted the technique of Smithwick<sup>23</sup> and most of our present operations are based on his procedure except that the twelfth rib is not resected, but the eleventh is in its entirety and that the two adjacent ribs are approximated with fine silver wire or No. 1 chromic catgut. The removal of the major splanchnic nerve from the mid thoracic level to the tip of the celiac ganglion

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### EXTENT OF SYMPATHETIC DENERVATION FOR HYPERTENSION

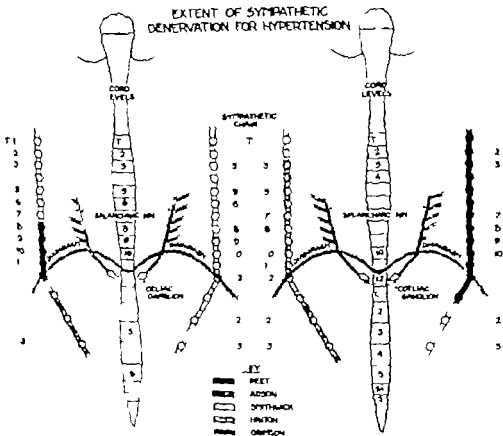


Fig. 2.—Extent for sympathetic denervation for hypertension. The presence of meet and add-on are unilateral those of 1/2 and 1/4 are transpleural. Grimson's operation described an atypical approach with extent of denervation used by 1/2 and 1/4 based on recent personal communication from these authors.

Obviously the mortality must rise with the extent of the operation and the acceptance of malignant or pre-malignant types of hypertension for operation.

Since 1940 we adopted the technique of Smithwick<sup>13</sup> and most of our present operations are based on his procedure except that the twelfth rib is not resected, but the eleventh is in its entirety and that the two adjacent ribs are approximated with fine silver wire or No. 1 chrome catgut. The removal of the major splanchnic nerve from the mid-thoracic level to the tip of the celiac ganglion

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the  
node

### FULMONARY COMPLICATIONS

Residual pneumothorax, atelectasis, and atelectatic pneumonia are predominantly dependent upon expert anesthesia which unfortunately is still not uniformly available. In most institutions, the director of anesthesia is fully trained and highly skilled, but the training program of anesthesiology has made an executive out of him with inexperienced residents actually administering intratracheal, positive-pressure anesthetics. This needs emphasis because our morbidity and mortality as observed in three separate series seems to depend mostly on the type of anesthesia the patient receives. Two deaths in 250 patients occurred on the operating table and were deaths from anesthesia.

Intercostal neuralgia, along the course of the resected eleventh rib, has been a real problem. Neither cutting crushing or injecting the nerve, nor leaving it intact or tearing it out with resection of the posterior root ganglion has seemed to make any difference. We have also tried paravertebral novocain injections and x ray to the paravertebral ganglia with indifferent results. Disturbance from this pain which radiates ventrally and caudally along the course of the nerve is a severe continuous back pain somewhat relieved by a fracture board, which seems to be due to a muscular insufficiency of the back. The sacrospinalis muscle, this potent splint of the spinal column, loses some of its attachments to the lower ribs when it is dissected medially and retracted. Many patients have spinal arthritis which seems to flare up, having lost some of the splinting support. If the vertebral end of the rib is not resected and the long muscles of the back are as little disturbed as possible this type of pain does not seem to occur as often.

Postural hypotension, postural dyspnea, and postural tachycardia are present with adequate denervation but are not disturbing after six to eight weeks. We have not found it necessary to prescribe elastic corsets and hose, but simply warn the patient not to rise suddenly and to keep moving. Shaving in front of a mirror in the standing position must be avoided for two months. Postural dyspnea is probably a mild coronary insufficiency due to poor venous return. Postural tachycardia is a useful compensatory mechanism to make up for the diminished stroke volumes which are demonstrable with the oscillometer. Its elimination by total sympathectomy has been demonstrated by Grimmon<sup>22</sup> but we are not convinced that a slow pulse under these conditions is of any advantage.

The subject of sterility in the male has been recently studied by Poppen and Lemon. It is certain that many hypertensive patients are impotent prior to operation. It is also true that this question should not be discussed unless the patient himself brings it up. Otherwise a paralytic inhibition is bound to complicate matters. One of us (G. de T.) with H. Hirsch<sup>22</sup> has presented evidence that motile spermatozoa may be present after resection of the dorsolumbar chain and the splanchnic nerves.

Lately attention has been focused on the fact that the visceral sensory afferent fibers of the upper abdomen are sectioned by sympathectomy for hypertension and so much so that one of us (G de T) with Walter<sup>11</sup> has recently reported the performance of splanchnic nerve sections for intractable pancreatic pain.

and of the sympathetic chain from the ninth dorsal to the twelfth lumbar ganglion inclusive is considered the *minimal procedure*. Nothing less than this is considered sufficient and it is felt that the postural hypotension which results from the addition of the lumbar sympathectomy is an important part of the operation. An extension of this procedure to include the dorsal sympathetic chain to the third or second dorsal ganglion seems indicated, when the hypertensive damage is far advanced, when there is considerable cardiac damage or angina but its disadvantages are also obvious. In the first place, the trans-thoracic approach through the tenth or the eighth rib carries a much higher morbidity than the retropleural approach; the number of pleural effusions at lotenes, and massive collapses is much greater. Second, such patient especially if they have a tendency to sweat perspire profusely in the neck and face and their heat regulating mechanism is considerably upset. Third the section of the cardiac accelerators, which run in part through the upper dorsal sympathetic ganglia prevents the postural tachycardia or the tachycardia following lung collapse and thus decreases the minute volume of the heart. This may throw a perfectly capable heart, whose venous return has been markedly decreased by the splanchnic section into failure resulting in pulmonary edema. Such was the case in a 50-year-old army officer in whom a bilateral trans-thoracic sympathectomy with removal of the chain from the third dorsal to the first lumbar level on both sides resulted in an acute heart failure immediately after the second stage.

One of us (O. C. J.) has been performing the high transpleural sympathectomies, without gaining the impression that the results were any better but recently we have become impressed with the suggestion of Poppen and Lemmon<sup>10</sup> who add the resection of the eighth rib to the eleventh and remove the sympathetic chain between the third or fourth dorsal to below the second lumbar segment retropleurally. If one were certain that the addition of the higher segments is essential this might become our routine procedure, but not enough time has elapsed to warrant the adoption of this procedure except for experimental purposes.

#### POSTOPERATIVE COMPLICATIONS

Elsewhere two of us (B. F. F. and G. de T.) will report on postoperative complications in detail.

#### CARDIOVASCULAR ACCIDENTS

*Cerebrovascular accidents* were observed in three patients, two of whom had visual phenomena and one a full blown cerebral thrombosis. *Cerebral thrombosis* was seen in one patient and *coronary insufficiency* occurred in five. We have seen no postoperative uremia, possibly because of our practice of not operating on patients with less than 50 per cent of the normal urea clearance (20 c.c. of urea clearance per 100 c.c. of blood).

These are probably insignificant sequelae in a group suffering from advanced cardiovascular disease.

TABLE II. RESULTS OF RENALISMO XEPH SECTION FOR ESSENTIAL HYPERTENSION IN 40<sup>th</sup> PATIENTS (FOLLOW-UP FROM ONE TO FIVE YEARS)

GROUP	NUMBER CASES	SUCCESS (PER CENT)	FAILURE (PER CENT)
1	33	83	15
2	123	73	25
3	24	0	100
Total	180	64	31

## THE ANALYSIS OF FAILURES

We have then 31 per cent failures, and the majority of these can be regarded as due to poor case selection. The results in all of the twenty four patients belonging to our third group were failures and for several years now the patients with malignant and premalignant types of hypertension have been regarded as inoperable and refused operation. It should be mentioned that both Peet and Isberg<sup>3</sup> and Smithwick<sup>20</sup> record good results in cases of malignant hypertension but it is our feeling that the malignant phase there was based alone on papilledema. We too have some startling results in a few patients with papilledema but no corresponding aacular damage in retinal, cardiac or renal vessels. Papilledema and high spinal fluid pressure per se do not place these patients in the inoperable group.

The analysis of failures indicates three reasons for the lack of success. Poor case selection has already been commented on. Insufficient denervation (less than the Lawrie-Smithwick procedure) seemed to be present in seven patients, and it was possible in three to improve the results by more extensive denervation. This was especially striking in one patient, in whom an infradiaphragmatic splanchnicectomy was done elsewhere, five years before with not even a temporary reduction in pressure and in whom five years later a generous supra-diaphragmatic resection resulted in marked benefit (grade II result).

In our first and second groups, there are nineteen patients, in whom shortly or at least within one year a recurrence or a dubious result was noted and of these the six failures noted in Group I are most important. These were young individuals with all the criteria of a vasospastic nonorganic arteriolar involvement who were sufficiently denervated and yet showed a progressive arteriolar disease uninfluenced by operation.

TABLE III. ANALYSIS OF FAILURES IN FIRST TWO PATIENTS, 1940 TO 1948

GROUP	CASES	PER CENT OF TOTAL	REASON
1		13	In-sufficient denervation
	31	25	Unexplained
			In-sufficient denervation
			Heart failure
			Stroke
			Unexplained
2	1	100	Poor case selection

\*The third group has been regarded as inoperable since 1940.



Other reports indicate that painless perforations of the duodenum may occur<sup>28</sup> or that reactivation of a gastric ulcer with massive hemorrhages can follow<sup>29</sup> splanchnic nerve section. We have not observed such a complication in this series and wish to emphasize that as soon as a peritoneal involvement occurs, somatic sensory stimulation would give danger signals. The increased gastroduodenal peristalsis which follows splanchnic section seems not to be experienced by the patients but lack of appetite or nausea at the smell of food may occur. Tincture of belladonna inhibiting the vagal preponderance eliminates such symptoms.

The mortality in this series was 9 in 230 patients, less than 1 per cent. As stated before, both patients died during the operation, obviously from bronchial obstruction. In the series of two institutions, there has been no mortality whereas in the third institution the department of anesthesia is just being reorganized.

#### OUR RESULTS

This report is based on the study of 230 hypertensive patients who can be grouped as shown in Table I.

TABLE I. GROUPING OF PATIENTS OPERATED UPON 1934 TO 1946

GROUP	NUMBER	TOTAL
1	57	171
2	171	
3	24	
TOTAL	252	

Of the 171 patients analyzed as resulting in failures, dubious benefit, marked improvement and complete remission. Failure was recorded when the blood pressure returned shortly or within a year to the preoperative level and symptoms were unimproved. Dubious benefit was noted when the results were not heart-satisfactory and blood pressure improved but not registered, 100 and 110 mm of mercury when symptoms subsided and no longer a complete remission of hypertension was recorded when blood pressure returned to below 140/90 mm of mercury for at least one year when symptoms subsided and when earning power was fully restored.

Our results were recorded according to the groups of hypertension and the four types of results. Of the 202 patients analyzed, the 139 patients, or 69 per cent of the total had either a complete reduction of blood pressure to normal or near normal and were regarded as having successful result. The remaining 63 patients were regarded as failures.

The results were obtained as shown in Table II.

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The causes for failure here are mostly speculative although some suggestive data are accumulating. In the first place it is possible that pheochromocytomas or cortical adrenal tumors have been overlooked. In the high transthoracic types of approach, this might be all the more possible since one cannot explore the subdiaphragmatic structures. Second, a corticoadrenal activity may well be the dominant factor in some hypertension even without visible or palpable enlargement and it is not known that splanchnic section would influence such a process, which no doubt is mediated through the corticoadrenal hormone of the pituitary. Finally we have seen and reported the case of one patient who showed no reduction in blood pressure following splanchnic section, who died suddenly two years after operation, at the age of 22 years, and in whom a complete autopsy revealed no anatomic cause for death or for the hypertension.

In our present state of knowledge then, we must admit that a certain small group of patients, even although their organic damage is slight, does not respond to splanchnic nerve section and that future work will have to elucidate the mechanism of this type of hypertension. Such work is now in progress.

## SUMMARY

A group of 250 patients have been followed for at least one year and not more than six, in whom the minimal procedure consisted of a total splanchnic nerve section with removal of the sympathetic chain above the ninth dorsal and below the second lumbar ganglia. More extensive procedures were tried in a selected group of patients but nothing can be said as yet about their being superior; the morbidity certainly rises with their use. The patients were grouped as being in an early, marked, and too advanced stage. For five years now none of the last group has been accepted. There were two anesthetic deaths in this series and no postoperative mortality. The results were excellent in the first fair in the second, and poor in the third group. The possible role of a cortico-adrenal factor in the maintenance of essential hypertension is stressed in such early cases in which splanchnic section has not been successful.

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We find that severe postoperative distention can be avoided in the average case by the administration of Prostigmine and the use of a rectal tube at four hour intervals. If the stomach is distended at operation we do not hesitate to pass a well lubricated nasogastric tube and leave it in place connected with suction for a day or two postoperatively.

A third postoperative death was caused by cardiac failure. This was a case of Banti's syndrome in a 67 year-old woman who also suffered from hypertensive cardiovascular disease. The patient died on the fourth postoperative day. In retrospect we wonder if the patient would have benefited from early digitalization.

Our first major error in clinical judgment in the selection of cases for operation arose in a case of posthepatitis cirrhosis. A brief summary of this case serves to emphasize important factors governing the selection of cases for operation in this important group.

#### CASE REPORT

A 29 year old man, on Feb. February 1943 developed epigastric discomfort, anorexia, and diarrhea with the passage of clay-colored stool. Coincident with these symptoms he developed pain and swelling of the legs.

The patient was admitted to the Presbyterian Hospital, March 1, 1943. On examination he was found to be slightly jaundiced. There were small tender nodules noted on each thigh. Biopsy of one of the nodules proved to be due to sporotrichosis. Further laboratory studies revealed serum bilirubin of 4.5 mg. per cent, serum phosphatase 9.1 Bodansky units, erythrocyte sedimentation test 3+, serum albumin 4 per cent, serum globulin 5.4 per cent, erythrocyte sedimentation rate 3 per cent, Rhine 4, Wassermann—alcoholic negative, cholesterol 3+. The prothrombin time was 73 per cent of normal. The patient had an afibrile course in the hospital but the jaundice and anorexia persisted. One month after admission the legs were no longer swollen as present but the iliofemoral glands could not be palpated. Laboratory findings were as follows: erythrocyte sedimentation rate 3+, erythrocyte sedimentation rate 9.2, hemoglobin 13 Gm., red blood cells 4,910,000, white blood cell 4,330, platelets 140,000, prothrombin time 73 per cent of normal, serum bilirubin 3.5 mg. per cent, serum protein 7.8 per cent, albumin 1 per cent, globulin 6.8 per cent. May 1, 1943, examination revealed the following: short period of pain, leukocytes fell to 29, hemoglobin

rose occurred within three months after onset of the patient's illness. Fourteen days after onset of anorexia a repeat x-ray film revealed the presence of esophageal strictures. The serum albumin fell to 1.8 per cent and the prothrombin time to 80 per cent of normal. Intravenous hypotonic acid liver function test revealed 0.8 Gm. excreted at the end of one hour. The patient's course for 4 months in the hospital was summarized as follows: severe postoperative anorexia.

In view of these findings we considered the question of esophageal portacaval anastomosis. It was our first experience with this type of case and proved to be a better one. On June 1, 1943, approximately three months after onset of the hepatitis, we operated upon the patient performing an end-to-side anastomosis of the portal vein to the vena cava. The patient very promptly developed cholelithiasis and was dead on the third postoperative day.

The most informative necropsy findings were in the liver. This organ presented the picture of healing subacute yellow atrophy (hepatitis) in which areas of nodular hyaline are interspersed with the areas of liver cell degeneration. There was no evidence of systemic manifestations.

## PORTACAVAL ANASTOMOSIS

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THE operation of establishing an anastomotic junction between the portal and caval systems (portacaval shunt) for the relief of portal hypertension has now been accomplished by us in thirty-six cases. There have been five postoperative deaths. Aside from the development of technique the experience has profited us most in the selection of cases for operation, the preparation of patients for operation, and their postoperative care.

Analysis of the five postoperative deaths and their contributions to our knowledge would seem worth while. One death from hemorrhage at the conclusion of the operation served, early in our experience, to emphasize the necessity for careful hemostasis. In this case a small vein in the great omentum had been torn and gone unobserved for a considerable period during the latter part of the operation.

Mesenteric thrombosis was the cause of death on the sixteenth postoperative day in a case of Banti's syndrome with a splenorenal anastomosis. This case was indeed a serious challenge to us of the advisability of continuing with the portacaval shunt procedure. A critical analysis of the case however revealed several points of interest. First, the anastomosis had been performed with meticulous care as to good blood vessel technique, asepsis, etc. It had been noted at the time however that the splenic vein was very large, thin walled, and sclerotized in areas whereas in other areas there were sclerotic plaques and in some places reduplication of the intima. Upon opening the anastomosis, blood was seen to flow from the splenic vein to the renal vein. The patient was allowed to be ambulatory early postoperatively and on about the sixth postoperative day distention of the abdomen with gas became progressively worse. This was followed by the appearance of sweats and increasing pain. Finally by the fourteenth postoperative day the patient had a high temperature and during the next two days became moribund. We have noted in some other cases of Banti's syndrome degenerative changes in the splenic vein but not nearly so extensive as in this case. Largely on account of this fact we have instituted anticoagulant therapy postoperatively in cases where we can attain a reasonably dry operative field. With the organization of an anticoagulant team in the Presbyterian Hospital we have been able to carry out this therapy without serious mishap.

The case of mesenteric thrombosis served to point up two other factors in the postoperative handling of cases of portacaval anastomosis, namely: (1) control of postoperative distention and (2) avoidance of early mobilization. It is our belief that a change in position from lying to upright before the soft tissues about an anastomosis have become stabilized by healing may well result in a slight shift of the soft parts, sufficiently to angulate or occlude by compression the anastomosed veins. Furthermore we are convinced that severe distention of the abdomen may accomplish the same undesirable result.

It was decided that the only hope for the patient was to attempt a portacaval anastomosis with removal of the very large spleen. Accordingly she was transferred to the Presbyterian Hospital. Operation was scheduled for May 1 and during induction with ether anesthesia the patient developed severe pulmonary edema necessitating postponement of the procedure in view of the prompt recovery and the absence of cardiac pathology it was concluded that the anesthesia (ether) may have precipitated the attack of pulmonary edema.

During the ensuing ten days the patient received ten transfusions and two 100 cc. doses of RhoGam intravenously. On May 13, 1941 under cyclopropane anesthesia the spleen was removed and the stump of the splenic vein anastomosed with side by side ligature, with the left renal vein. At operation the liver was found to be severely contracted and nodular. The spleen was five times normal size and the portal pressure measured 450 mm. Hg. The patient's systemic blood pressure was well maintained throughout the operation and she left the operating table in good condition. Heparin was given intravenously at the instant of opening the anastomosis and antirheumatic therapy was maintained for nine days postoperatively. During postoperative convalescence the patient received 500 cc. of blood, 500 cc. of plasma, and 75 Gm. of albumin intravenously. There were no signs or evidence of acute liver failure during convalescence.

Our fifth postoperative death taught us much concerning the selection of cases of portal cirrhosis for operation. The case is described here.

#### CASE REPORT

A 49 year old man previously had had eight abscesses of the Prael term Hospital for phlebotomy procedures to restore some back had part been destroyed by a gamma. In November 1915, the patient developed pain in the epigastrium coincident with back aches appeared. He gave long history of moderate daily consumption of alcohol with not infrequent episodes. He had been treated for syphilis from 1925 to 1941. There was no history of jaundice. Appetite had never been good.

Examination of this patient on admission revealed large bladder (ascites) with wasting of the soft parts elsewhere. There was no jaundice but numerous spider angiomas were present. Following removal of 5,500 cc. of white fluid, a hard liver could be felt just to the costal margin. The spleen was not palpable.

The significant laboratory findings at the time were cephalin flocculation serum protein 5 per cent albumin 1 per cent globulin 3 per cent prothrombin time 55 per cent of normal bromocresol green retention thirty minutes, 60 per cent. The presence of esophageal varices as demonstrable by ray examination.

After six weeks on modern curative medical regime the patient's weight began to improve. He gained ten pounds in eight weeks. There was very slight rise in blood proteins (albumin 3 per cent, globulin 5 per cent) but no appreciable lessening of the ascites. After four months therapy there was no lessening of ascites. The cephalin flocculation test remained serum protein 5.5 per cent, albumin 0 per cent, globulin 0 per cent. After five months therapy serum protein was 5.2 per cent, albumin 0 per cent, globulin 0 per cent. The diuretic drugs so proteins resulting from the removal of 4 to 7000 cc. of white fluid every five to seven days was beginning to show on the total protein figure but was to follow the progressive decline in liver compensation— for the first time the blood albumin content had become lower than the globulin content.

After nine months therapy the patient had no diuresis in the winter. Whereas the bromocresol green retention 10 per cent less than in the fall (40 per cent after three months) the blood proteins had on a fairly decreased albumin 4 per cent, globulin 6 per cent. The painless removal constant (intravenous) was 50 per cent of normal (2). Interestingly enough, however the cephalin flocculation test had previously consistently had decreased. The prothrombin time had not decreased as terribly over the nine month period of observation.

On Sept. 25, 1941 approximately ten months after the first episode of cirrhosis had appeared in this patient splenorectal anastomosis employing the non-tissue technique

Dr. Allen Whipple very kindly joined me in consultation. The Rockefeller Hospital to help make decision in this difficult case.

Whereas, from the clinical course prior to operation, it seems very improbable that this man would have recovered, on the other hand, it was an error to have operated upon him when we did. The persistently elevated cephalic flocculation test should have warned us of the presence of active hepatitis. The progressive fall in serum albumin to an extremely low level, the rise of the prothrombin time to high levels, and the marked retention of bromsulfalein were additional warnings of serious liver decompensation. The wiser course to have pursued in this case would have been to have replaced the blood losses from hemorrhage by transfusions with the hope that he would recover sufficient liver compensation to withstand a portacaval shunt procedure at some subsequent date. This case came along early in our experience, subsequently we have operated successfully upon a fair number of patients with posthepatitis cirrhosis. Unfortunately it would seem that cirrhosis with portal hypertension is not an uncommon sequela to hepatitis.

I shall cite a recent case to illustrate that posthepatitis cirrhosis cases present the same threat of sudden death from hemorrhage as do cases of portal cirrhosis of the avitaminous (alcoholic) type.

#### CASE REPORT

A girl 18 years of age in 1941 had infectious hepatitis, slight jaundice with excrete 11.0. Four years later (November 1945) the patient had the first episode of gastrointestinal bleeding. This was followed by ascites. In January 1946, the patient was admitted to the Rockefeller Hospital for special study and treatment. She improved gradually with total disappearance of the ascites. In the fall of 1946 she had returned to college. She suddenly in October she suffered from severe hemorrhoids. In spite of intravenous glucose transfusions, and intravenous liver extract, she lapsed into coma. Gradually after three days the coma began to clear. The ascites which had supervened was relieved by one paracentesis followed by several intravenous injections of serum albumin. The patient then did well until December 1946, when she had the third episode of gastrointestinal bleeding. Following recovery from this, a liver biopsy was done. The liver was found to be markedly contracted and studded with large and small nodules. The small areas of regenerated liver cells were unevenly distributed with intervening masses of fibrous tissue. On Jan. 9, 1947 the patient had another spell of gastrointestinal bleeding. At that time the hematocrit fell to 23. In spite of five transfusions the patient lapsed into coma from which she gradually recovered. On March 8, 1947 the patient suddenly developed an unexplained fever. Temperature rose to 103° F. Following the fever, ascites supervened which was gradually cleared with intravenous albumin. Unfortunately however following the last dose of albumin the patient had the fifth attack of gastrointestinal hemorrhage requiring four transfusions. To summarize, this girl had four episodes of severe gastrointestinal bleeding over five month period. The spleen had been appreciated as unusually large throughout this period and as evidence of hypersplenism she maintained leucopenia, low platelet count (14,000) and secondary anemia. On the other hand the albumin globulin ratio was not reversed. The serum albumin ranging better than 3 per cent the bromsulfalein retention as only 23 per cent after forty-five minutes. The disconcerting findings concerning the liver were maintained cephalic flocculation, the episode of coma, and the more recent (March) unexplained fever in the presence of jaundice. The prothrombin time as slightly elevated, finding back in view of the good serum albumin level, we did not interpret as necessarily indicating liver decompensation. We have recorded moderate elevations of the prothrombin time in cases of portal hypertension with hypersplenism before—even cases of extrahepatic portal block in which the liver chemistry was normal.

# CAUSALGIA

## III A GENERAL DISCUSSION

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THE painful condition following injury of peripheral nerves which we recognize as causalgia must have occurred from the earliest times. Its incidence in civilian life has undoubtedly been increased by the dangers associated with the more general and widespread use of industrial machinery, rapid means of transportation, and similar hazardous accompaniments of our modern civilization. It is a disorder however which has confronted the medical profession in particularly large numbers periodically as we have allowed ourselves to become embroiled in mass warfare. As each succeeding war tends to result in larger numbers of nonfatal battle casualties and as improved methods of treatment result in the conservation of more and more injured extremities, the problem of causalgia becomes of increasing military importance.

It is my purpose to discuss some general aspects of the problem of causalgia in the light of the early contributions and of recent studies. An attempt will be made to clarify the clinical picture and the treatment and to make some comments concerning theories of the basic mechanism of pain. I shall also try to point out certain lines of investigation which I feel may contribute to our further understanding of this disorder.

I do not know who first observed and recorded this clinical syndrome. Certainly Denmark, in 1813 described some features of the condition very accurately. Speaking of a soldier who had sustained a radial nerve injury from a musket-ball wound of the arm, he said:

I found him labouring with severe pain which the largest opium could not manage. That he kept his hand, if it could be called such was disturbed by frightful dreams and starting. He described the sensation of pain as beginning at the extremities of the thumb and of the fingers, except the little one and extending up the arm to the part wounded. It was of burning nature he said, and so violent it caused continual perspiration from his face. He had excoriation on the palm of the hand, from which exuded a serous discharge. The cause of this he ascribed to shells rolling over it. His gashes he observed, were insufferable depriving him of sleep and the enjoyment of his food for which he had sometimes an appetite. He declared himself incapable of enduring it longer than some relief and earnestly requested the removal of his arm.

The author further pointed out that touching or moving passively the affected hand caused exacerbation of the pain. After futile effort to alleviate the pain with warm and vapour baths, and ne embrocations, etc., an amputation was carried out with complete relief. Denmark had dreamed with the patient the possibility of saving the limb and relieving the pain, by cutting down upon the nerve and removing a part of it above the wound.

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as performed. At operation the liver was found to be nodular and extremely turgid. The spleen, dilated and approximately three times normal size. Measurement of the portal pressure revealed that it is in excess of 300 mm. H<sub>2</sub>O after

The patient was given ether anesthesia. Early in the operation the blood pressure began to fall in spite of more than restitution of the blood loss. All in all the operation was accomplished with minimal blood loss and I record time in spite of which the patient was in poor condition at the close of the operation.

The patient lived four days postoperatively, the last thirty-six hours of which he was in coma. The terminal picture of failing liver.

Reviewing the case in retrospect, there is no denying that the patient was doomed without operation. He had had thirty-nine paracenteses and for months had begged for surgical relief. Whereas he was entitled to an attempt at surgical relief the important question arises, what could we have done to increase the chances of his survival? We now know of several things we might have done to increase this man's chances of surviving a portacaval shunt procedure: (1) The use of cyclopropane anesthesia. We are now convinced that this is by far the best anesthetic for poor risk patients with cirrhosis. (2) Preoperative and postoperative intravenous albumin therapy. We now have evidence that a blood albumin raised to a figure in excess of 3 per cent in a badly cirrhotic liver by the intravenous administration of albumin is likely to maintain this rise for a considerable period of time that is, period of time far in excess of that which can be accounted for on the basis of the amount of albumin in grams given. (3) The early use of Prostigmine at four hour intervals postoperatively for the control of distention.

In conclusion we may summarize some of the most important information we have gleaned from our experience as follows: (1) The necessity for scrupulous hemostasis and the desirability of postoperative anticoagulant therapy. (2) The avoidance of operation in the presence of active hepatitis in cases of cirrhosis secondary to hepatitis. As our experience has shown cirrhosis with evidence of portal hypertension may occur in some cases of infectious (viral) hepatitis before the latter is subdued. (3) The avoidance or postponement of operation in cases of cirrhosis, whatever the cause, when the liver is bordering on decompensation. It is not safe to rely too much on clinical signs unless they are confirmed by laboratory findings—jaundice for example of a slight degree may come and go in patient with cirrhosis but a deepening jaundice with an elevated cephalin flocculation would caution me not to delay. Furthermore it is true that some cirrhotic patients may have the most extreme depression of blood albumin, bromsulfalein and other tests without a trace of jaundice. The sudden appearance of telangiectasia (spider angiomas) would justify a re-examination of the liver at this time before proceeding with operation.

In general, a patient with chronic cirrhosis who consistently shows an albumin between 2.5 and 3 per cent with a bromsulfalein retention in excess of 40 per cent thirty minutes after injection with or without an elevated prothrombin time is not a good risk for the portacaval shunt. Unfortunately all too often

cases present themselves in which operation offers the only ray of hope.

# CAUSALGIA

## III A GENERAL DISCUSSION

HARRIS B. SHUMACKER, JR. M.D. INDIANAPOLIS, IND.

(From the Department of Surgery, Yale University School of Medicine, New Haven, Conn.)

THE painful condition following injury of peripheral nerves which we recognize as causalgia must have occurred from the earliest times. Its incidence in civilian life has undoubtedly been increased by the dangers associated with the more general and widespread use of industrial machinery, rapid means of transportation, and similar hazardous accompaniments of our modern civilization. It is a disorder however which has confronted the medical profession in particularly large numbers periodically as we have allowed ourselves to become embroiled in mass warfare. As each succeeding war tends to result in larger numbers of nonfatal battle casualties and as improved methods of treatment result in the conservation of more and more injured extremities, the problem of causalgia becomes of increasing military importance.

It is my purpose to discuss some general aspects of the problem of causalgia in the light of the early contributions and of recent studies. An attempt will be made to clarify the clinical picture and the treatment and to make some comment concerning theories of the basic mechanism of pain. I shall also try to point out certain lines of investigation which I feel may contribute to our further understanding of this disorder.

I do not know who first observed and recorded this clinical syndrome. Certain Denmark, in 1813, described some features of the condition very accurately. Speaking of a soldier who had sustained a radial nerve injury from a musket-ball wound of the arm, he said:

I found him labouring under severe pain, both the largest part could not move. The little finger had if it could be called such, and started by frightful dreams and starting. He described the position of pain as beginning at the extremities of the thumb and all the fingers, except the little one and extending up the rest of the part wounded. It was of burning nature, he said and so violent that cause no sleep and perspiration from his face. He had excoriation on the palm of the hand, from which issued an enormous quantity. The cause of this he described as shell rolling over it. His agonies, he observed, were such that he could not find for him to keep it long.

The author further pointed out that touching or moving painful the affected hand caused exacerbation of the pain. After futile efforts to alleviate the pain with warm and vapour baths, anodyne embrocations, etc., an amputation was carried out with complete relief. Denmark had discussed with the patient the possibility of saving the limb and relieving the pain, by cutting down upon the nerve and removing a part of it above the wound.

Presented at the annual meeting of the Society for Vascular Surgery, Atlantic City, N. J., June 9, 1947.

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In 1838 Hamilton described a peculiar redness of the skin, swelling, and contractures in certain cases of intense pain associated with partial paralysis of peripheral nerves. From the account of his patients it is evident that they were not examples of true causalgia as we now recognize this state.

Paget in 1864 described fully the glossy skin which may be associated with causalgia and pointed out its association with pain :

Glossy fingers appear to be a sign of peculiarly impaired nutrition and circulation due to injury of the nerves. They are not observed in all cases of injured nerves, and I cannot tell which is the peculiar condition of the cases in which they are found; but they are a very notable sign, and are always associated, I think, with distressing and hardly manageable pain and disability. In well marked cases, the fingers which are affected (for this appearance may be confined to one or two of them) are usually tapering smooth, hairless, almost void of wrinkles, glossy pink or ruddy or blotched as if with permanent chilblains. They are also very painful, especially on motion, and pain often extends from them up the arm.

Though Paget recognized the association of glossy skin and a painful state, there is nothing in his discussion which would lead one to believe that he recognized or referred to the peculiar condition which we know as causalgia.

In the same year appeared the monumental treatise on *GunsHOT Wounds and Other Injuries of Vertebrae* by Mitchell, Moorehouse, and Keen which contained their classic account of the disorder to which Mitchell subsequently applied the term "causalgia." So vivid is their depiction of the condition that I feel justified in quoting them at some length.

If there are reasons we have set apart for distinct consideration that kind of pain which we have before spoken of as burning pain. It is a form of suffering as yet undescribed, and so frequent and terrible as to demand from us the fullest description. The terms here used may seem strong to those who have not encountered these cases but so, so who has seen them will think that, as regard some of them, it would be possible to overstate their most wretched condition.

We have some doubt as to whether this form of pain ever originates at the moment of the wounding but we have been so informed as regards two or three cases. Certain it is that as a rule the burning rises later but almost always during the healing of the wound.

The seat of burning pain is very various, but it never attacks the trunk, rarely the arm, thigh, and not often the forearm or leg. Its favorite seat is the foot and hand. In these parts it may be found most often where the nutritive changes are most with that is to say in the palm of the hand, palmar surface of the fingers, and in the dorsum of the foot scarcely ever on the sole of the foot or the back of the hand. Where it first existed in the whole foot or hand, it always remained here in the parts referred to, as its favorite sites.

The great mass of sufferers described this pain as superficial but there said it was also in the joints, and deep in the palm. If it lasted long, it was referred finally to the skin alone.

Its intensity rises from the most trivial burning it starts if it rises, which can hardly be credited, but which reacts on the whole economy until the general health is seriously affected.

The part itself is not alone subject to an intense burning sensation, but becomes exquisitely hyperaesthetic so that touch, the slightest touch of the finger is

increases the pain. Exposure to the air voided by the patient with a care which seems absurd, and most of the bad cases keep the hand constantly wet, finding relief in the moisture rather than in the coolness of the application.

As the pain increases the general sympathy becomes more marked. The temper sours and grows irritable, the face becomes anxious, and has a look of weariness and suffering. The sleep is restless and the constitutional condition reacting on the wounded limb exacerbates the hyperaesthetic state so that the rattling of newspaper, breath of air, no other step across the ward, the vibrations caused by military band, or the shock of the feet in walking give rise to increase of pain. At last the patient grows hysterical, if we may use the only term which covers the facts. He walks carefully, carries the limb tenderly with the sound hand is tremulous, nervous and has all kinds of expedients for lessening his pain. In two cases, at least, the kin of the ure body became hyperaesthetic when dry and the men found some ease from pouring water into their boots. They said, when questioned that it made walking hurt less but how or why unless by diminished vibration, we cannot explain. One of these men went so far as to wet the sound hand when he was obliged to touch the other and insisted that the beard should also wet his hand before touching him, complaining that dry touch always exacerbated his pain.

Cold weather usually eased these pains, heat and the hanging down of the limb made them worse. Motion of the part was more durable in some of the very worst cases, but for the most part it did no harm, unless so extensive as to flush the injured region.

The relations of burning pain to altered nutrition already received attention from us. It appears quite certain that cases of glossy skin, burning all way exists. It is also certain that it may exist without association with diseased skin, but that in these instances the evidence of depraved nutrient states will be very likely to follow upon the pain, should that symptom last very long.

The temperature of the burning part we have always found to be higher than that of surrounding part or than that of corresponding point on the half of the body.

Mitchell and his associates elaborated further upon the glossy skin previously described by Paget. They found the skin deep red or red and glist in patches, the epithelium often partially denuded, leaving the cutis exposed in places, the subcuticular tissues generally shrunken, the integument tightly drawn and often cracked. They described the skin as shining as though it had been skillfully varnished. In most patients the affected part was devoid of hair. In some a vesicular eczematous eruption was present, often recurring from time to time. The nails were curved with extreme lateral arching, with thickening of the skin underneath the end of the nail, and sometimes with retraction of the proximal end so as to leave sensitive matrix partly exposed. In their experience canneling always occurred in cases of partial, and never in cases of complete division of nerves. In the description of affected cases, darting pricking, tingling and other pains were described in addition to burning.

#### FURTHER COMMENTS ON THE SIGNS AND SYMPTOMS OF CAUSALGIA

From the foregoing it is apparent that causalgia as originally described was characterized by the following features: pain of varying intensity and predominantly burning in character coming on some time after incomplete injury

In 1838 Hamilton described a peculiar redness of the skin, swelling, and contractures in certain cases of intense pain associated with partial paralysis of peripheral nerves. From the account of his patients it is evident that they were not examples of true causalgia as we now recognize this state.

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For these very reasons we have set apart for distinct consideration that kind of pain which we have before spoken of as burning pain. It is a form of suffering as yet undescribed, and so frequent and terrible as to demand from us the fullest description. The terms here used may seem strong to those who have not encountered these cases, but no one who has seen them will think that as regards some of them, it could be possible to overstate their most tormented condition.

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to a peripheral nerve, felt chiefly in the periphery of the affected extremity exacerbated by touching the part, dependency jarring emotional excitement, dryness, and generally by heat, relieved somewhat by wetness and cold, associated usually with glossy red, blotched skin, always comparatively increased in warmth and leading in many instances to emotional instability. In its essentials this has remained an accurate description of the condition. In certain details, however further experience has revealed aberrations from this original account. For example it has been evident for some time that the affected hand or foot is not invariably warmer but sometimes colder than the contralateral one.

Elsewhere my associates and I have presented our experiences with regard to the signs and symptoms of causalgia. Much valuable information concerning the clinical features of this disorder has been presented in other reports of cases which were studied in the Armed Forces during World War II. It may be profitable to analyze these data.

As experience with causalgia has increased through the years it has become a generally accepted fact that this condition is particularly prone to occur following injury of the median or sciatic nerve. There was some involvement of the median nerve in 39 of our 49 cases of causalgia of the upper extremity and of the sciatic nerve in 34 of 41 cases involving the lower extremity while the tibial or peroneal divisions were affected in an additional 5 cases. It is of interest, however that the ulnar nerve was injured in this series almost as frequently as was the median (37 cases as compared with 39). I have listed in Table I the available data on 230 recently reported cases.<sup>4-10</sup> In 80 of the 97 cases of causalgia of the lower extremity (82.5 per cent) the sciatic nerve was injured while the tibial and peroneal nerves were damaged alone or in combination in 11 of the remaining cases. In the upper extremity the median nerve was affected more frequently than any other nerve though the brachial plexus and various

TABLE I. UPPER LIMBS AND LOWER

NERVES INVOLVED	THOMAS & WATKINS REPORTS					TOTAL CASES
	MEAN NERVE DIVISION	ULNAR & PERONEAL	ULNAR & MEDIAN	NERVE IN EXT. L.	MEAN NERVE DIVISION	
Brachial plexus	1		1	3	14	20
Median, brach & radial			3		11	14
Median	7	7	9	14	7	44
Median & ulnar	1	3			7	11
Median & radial			1		1	2
Radial				1	4	5
Ulnar		1			4	5
Radial & ulnar			1	17	3	11
Sciatic	4				27	74
Sciatic & peroneal					1	1
Peroneal				3		3
Tibial		1			3	4
Tibial & peroneal			2			2
Peroneal			1			1
Total	13	11	21	20	60	125

combinations of its three chief nerves were involved even more often. In the recent war causalgia occurred more commonly in the upper extremity than in the lower. In a total of nearly 400 cases (Table II) the upper extremity was affected in 238 or 60 per cent.\*

TABLE II. I. OCCURRENCE OF CAUSALGIA IN UPPER AND LOWER EXTREMITIES

AUTHOR	EXTREMITIES INVOLVED	NUMBER OF CASES	TOTAL CASES
	UPPER	LOWER	
Mayfield & Devine	8	8	16
Ulmer & M. Schell	1	79	80
Rasmussen & Freedman	82	18	100
Albritten & Maltby	23	44	67
Goodman et al	11		13
Erikson et al	25	70	95
Shumacker et al	49	41	90
Total	238 (60%)	139 (40%)	377

All of the cases described by Mitchell and his associates were examples of partial paralysis of nerves and certainly most of those subsequently reported have had incomplete nerve lesions. It has become evident, however, that causalgia may occur following complete paralysis. Pollock and Davis<sup>13</sup> observed that burning pain occurred once in their series of 38 cases in the presence of a complete lesion of the ulnar nerve. Leriche<sup>14</sup> and Freeman<sup>15</sup> have observed causalgia in the distribution of a nerve which had been completely divided, and Albritten and Maltby found the nerve completely divided in 2 of their patients. In our series of 90 cases the nerve injury was clinically complete in 11; these patients had neuromas in continuity to be sure and in none was the nerve found at operation to be divided with separation of the cut ends. Of perhaps similar significance is the fact that division and resuture of nerves is often ineffectual in bringing about relief of pain.

All of the recent observations emphasize the hazard of final evaluation of the status of peripheral nerve function from examinations carried out before relief of pain. Such examinations notoriously yield unreliable information, the apparent extent of nerve damage generally appearing much greater than is evident when the examination is repeated after pain has been eliminated. This observation is of some importance in reference to the question whether one's initial attack in causalgia should be directed toward relief of pain or to surgical attack upon the seemingly injured nerves.

Mitchell, Moorehouse, and Keen's skepticism concerning the occurrence of causalgic pain immediately after wounding is not borne out by recent studies. It is true that the patient's memory for details during and immediately after such a trying experience may be inaccurate. Nevertheless, approximately 50 per cent of patients with causalgia stated that the onset of pain was immediate. This was true in 36 of 98 patients reported by Rasmussen and Freedman, 44 of 75 reported by Ulmer and Mayfield, and in 50 of our 90 patients. Most of the other patients noted beginning of pain within the first week after injury.

In all of the patients studied by Mitchell, Moorehouse, and Keen the pain was described as burning in character though other types of pain were also



often present. It was the constancy of burning pain which led Mitchell to designate the clinical syndrome *causalgia*. Though burning is the usual and characteristic type of pain, otherwise indistinguishable cases in which the patient does not describe the pain as burning are occasionally seen. Thus absence of burning was found in about 10 per cent of the patients studied by Kirklin, Chenoweth, and Murphy and in 4.4 per cent of our patients. The only report with which I am familiar which includes a large number of cases of *causalgia* without burning pain is that of Rasmussen and Freedman. 45 of their 100 patients did not have burning. It is of interest that, although these authors stated that the clinical picture in these 45 patients was otherwise nearly identical with that in the remainder they also said that the cases of minor *causalgia* reported by Homans were similar to their own. Most authors have not encountered cases of major *causalgia* without burning pain. Burning is certainly the common and predominant pain, but a small percentage of patients are seen who have no burning and are in every other respect suffering from typical *causalgia*. I do not feel that the absence of burning in such cases precludes a diagnosis of *causalgia* though etymologically the term is not strictly applicable to them.

In the original account it was pointed out that some relief of pain generally resulted from wet applications and often from exposure to cool weather. Such alleviation from moisture and cold has been encountered subsequently in a variable percentage of cases. Ulmer and Mayfield found that 68 of 75 patients experienced some relief and only 7 noted no effect from moisture. Almost one-half of the patients of Kirklin, Chenoweth, and Murphy obtained some amelioration of pain from local use of a wet cloth. Forty-four of the 100 patients studied by Rasmussen and Freedman had tried cold wet applications on their own initiative; 35 noted partial relief and 9 no effect. In our own series, alleviation of pain from moisture was experienced by only 17 of 90 patients. It has been the common finding that those patients with vasodilatation are apt to prefer cold and those with vasoconstriction warmth. Vasodilatation of the injured extremity was present in most of the patients of Rasmussen and Freedman and three-fourths of them had less pain on cool rainy days. Fifteen of our patients obtained some relief from cold wet applications or from cool weather. 1. had some increase in warmth of the affected hand or foot. Four of the 7 patients who had amelioration from warm moist poultices or from warm weather showed evidence of vasoconstriction. It must be concluded that wet applications are by no means always effective in providing partial relief. Though warmth often helps those patients with vasoconstriction, and cold those with vasodilatation, there are many exceptions. Indeed 64 of our 90 patients noted no amelioration of pain from any environmental alteration. Kirklin, Chenoweth, and Murphy have emphasized the well supported observation that such alleviation of pain is not a constant nor diagnostic feature of *causalgia*.

Though relief of pain from changes in the environment does not appear to be a constant feature of *causalgia*, alleviation of pain during sympathetic anesthesia seem to be characteristic of the disorder. This is a point recently emphasized by Doupe, Cullen, and Chanee.<sup>22</sup> I have encountered nothing in recent reports or in my own experience to bring into question the validity of this feature of *causalgia*.

Kirklin and his associates have called attention to the constancy of exacerbation of pain from certain stimuli in all cases of true causalgia. In their experience, moving or touching the affected part, sudden jarring loud noises, and emotional excitement were common causes for marked, sudden increase in pain. Our experience is in entire agreement. Touching or tapping the hand or foot, moving it passively or having the patient use it actively were the commonest stimuli causing such reactions. The exaggeration of pain from touching the body, noises, hunger and emotional excitement occurred commonly in the severer cases of causalgia and less often in milder cases.

The pain of causalgia is apparently always constant except perhaps in those with the mildest cases and in those who are improving spontaneously or from treatment. It is always felt most intensely in the periphery of the extremity and commonly only in the peripheral sensory distribution of the affected nerve or predominantly in this area. Numerous examples are seen however in which the pain is also present outside the area innervated by the damaged nerve. Sometimes it tends to spread up the arm or forearm. As Mitchell and his associates originally pointed out, it is particularly likely to be localized on the palmar surfaces of the hands and fingers. In contrast to their observation, however we found it was often felt predominantly in the sole of the foot.

Their belief that glossy skin was especially common in causalgia and that such nutritive changes in the skin never occurred in the absence of burning pain has not been supported by other studies. Pollock and Davis, for example, encountered 41 cases of glossy skin unassociated with causalgia, and found glossy skin in only 8 of 38 cases of burning pain. Meigs and Benisty had felt that alterations in the muscles and in the articular and tendinous structures were the result of associated vascular lesions. Pollock and Davis however noted vascular lesions rarely in their cases. It has been my experience that glossy tight skin, as well as abnormal curving of the nails, periarticular fibrosis, contractures, and marked atrophy of muscles and subcutaneous fat are particularly common in combined neurological and vascular lesions. Mayfield and Devine and Ulmer and Mayfield pointed out an association of the state of the skin and hair with the vasomotor status. According to them the skin of those in vasodilatation was usually reddish, dry and scaly and the hair long and coarse while in those with vasoconstriction the skin was usually thin, glistening and the digits tapered and the hair diminished. Such observations were noted in some of our patients though we did not find this association as commonly as they. In our patients, absence of sweating was found to occur particularly in those with relatively complete sensory loss, though this was not invariably the case.

Mitch H. Moorehouse and Keen stated that the causalgic limb was always warmer than the contralateral one. For some time however it has been clear that some causalgic extremities present evidence of vasoconstriction. A survey of the literature reveals a rather amazing discrepancy concerning the occurrence of vasodilatation and vasoconstriction. Among the more recent reports, for example we note that Wan found vasodilatation and hyperhidrosis in his 20 patients, while Coolman, Mewinger and White encountered evidence of sympathetic overactivity with aggravation of symptoms in a cold environment in their 13 cases. Three of Mayfield and Devine's patients had coldness of the hand or

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this feature of *causalgia*.

ing which Mitchell and his associates first employed, almost every conceivable type of medication, physiotherapeutic aid, and surgical operation has been given a trial. Most of these measures have been followed by unreliable, inconstant results, or have proved entirely inefficacious. Some of them are needlessly destructive such as the complete division and resuture of an only partially injured nerve, extensive posterior root section, and cordotomy. I shall discuss particularly the role of sympathetic interruption in treatment, and especially the use of repeated procaine blocks and operations upon the ganglionated chain. Though successes have been reported with periarterial sympathectomy this method has proved less reliable than the more direct attack upon the sympathetic chain.

I feel no hesitation in re-emphasizing the worth of sympathetic interruption. Doubt still exists concerning the usefulness of procaine blocks, and though patients successfully treated by sympathectomy have been reported in the literature from time to time for nearly twenty years, this method of treatment has in general not found its way into the common source books of learning. A survey of 5 of the most recent textbooks of neurology<sup>2-6</sup> for example reveals that such methods are mentioned in only one. The comments concerning treatment are most discouraging. One states, "For persistently painful neuritis, and for causalgia, surgical intervention has justified itself. The procedures in vogue embrace neurolysis, resection and immediate suture, intraneural injections of alcohol, and periarterial sympathectomy. With each and all of these, favorable results have been secured. Another advises, 'Section of the nerve and suture may be required for permanent relief although the condition often passes away spontaneously in several months. Repeated infiltration of the peripheral fibers with novocaine may give permanent relief. When all other methods fail, rhizotomy or even cordotomy must be employed.' In another text we find the following: 'The treatment is extremely difficult. Most of the patients become addicted to opiates, as no other analgesics give relief. Many complain that the contact with the vessel in which the limb is immersed in warm water for relief causes more trouble than the relief is worth. When the pain is finally gone (in one or two years) or as soon as possible massage should be instituted. When causalgia is due to a neuroma, resection at a higher level may give relief. Injections of alcohol have been recommended, but in my experience they have not produced results. Cobra venom is usually of no avail. When the pain finally does cease the addict must be treated as a separate condition.' Still another states, 'The satisfactory treatment of causalgia is always difficult. The most effective method of relieving the pain is to excise the damaged portion of nerve and resuture it. This means, however, substituting for an incomplete lesion, complete one with prolonged and possibly permanent disability. On the other hand, if medical treatment is unsuccessful and operation is to be undertaken months after the injury, resection of the damaged portion of nerve may be of no benefit and the pain may persist even after interruption of the painful pathway by the cordotomy. Generally it is wise to begin with medical measures and review the position after a month or two. If he is not making progress, and especially if he is a neurotic individual, surgical treatment should be carried out. If operative treatment is decided upon, either the damaged rea-

foot with thin, glistening skin and excessive sweating, while in 9 there was elevation of skin temperature with little or no sweating and increased growth of hair. The further report of this series by Ulmer and Mayfield did not give precise data concerning the vasomotor status. They stated, however, that those patients with vasodilatation generally obtained relief from cold, moisture and vice versa, and that 38 patients preferred cold water 30 warm water and 7 noted no effect from moisture. Rasmussen and Freedman found that their early cases showed evidence of vasodilatation which sometimes persisted as long as six months, but that generally after several months moderate vasoconstriction ensued. This tendency for vasodilatation of the affected limb in early cases and vasoconstriction in cases of long standing has been mentioned by some observers in connection with other posttraumatic disorders of the Sudeck atrophy type. In the experience of others, however, who have recently reported on large series of cases of causalgia, no change in vasomotor status has been observed during rather long periods of observation.<sup>6</sup> My associates and I have made an effort to evaluate carefully the vascular status of our patients and though these studies were not as comprehensive as we should have desired them to be I feel that they permitted us to detect at least gross aberrations from the normal. We were rather surprised to find that about one-third of our patients presented evidence of relatively normal vascular tones. Most of the others had relative vasodilatation though some had distinct vasoconstriction. The vasoconstriction was rarely intense and the vasodilatation not often complete. Indeed, I have not found any significant difference in the vascular responses of causalgic limbs and of extremities with peripheral nerve injuries without causalgia. From the data available it appears that the affected hand or foot is likely to have increased warmth in causalgia just as in the noncausalgic extremity with injury of peripheral nerves, that in some cases vasoconstriction will be present, and that in a fairly significant percentage the vasomotor tones will be relatively normal.

The essential diagnostic criteria of causalgia appear to be the presence of constant spontaneous pain following partial or more rarely complete injury of peripheral nerves, generally but not always, predominantly burning in nature exacerbated by certain stimuli, and capable of temporary complete or nearly complete alleviation during sympathetic procaine anesthesia. These cardinal points, together with the other features which I have discussed, make the diagnosis of causalgia relatively simple and permit its easy differentiation from such related disorders as phantom limb and amputation stump pain, minor causalgia, Sudeck's atrophy and similar posttraumatic vasomotor states. Confusion exists only in the case of the few patients who have atypical causalgia-like states in whom one or more of the essential diagnostic findings are absent. These cases are difficult to fit into any one of the recognized clinical entities. It would appear wise for the present to designate them as cases of atypical causalgia.

#### TREATMENT

It is not my purpose to review here all the measures which have been tried in an effort to bring about relief in causalgia. Beginning with the local Nister

excellent. When there was persistence of some pain but when the patient's course was so favorably altered that no further treatment was required, I have considered the outcome as good. Under poor are listed the few instances of trivial relief or of complete failure. Some of the failures undoubtedly occurred in examples of atypical and not true causalgia as was the case in the single failure in our own experience.<sup>4, 20</sup> It is evident that excellent results were obtained in 196 patients, or 76.3 per cent; good results in 54, or 21 per cent, and poor results in only 4, or 1.7 per cent. Excellent results are somewhat more frequent in causalgia of the upper (82.9 per cent) than in causalgia of the lower extremity (65.6 per cent). In our own experience it appeared clear that the results were better in cases of severe causalgia than in the milder cases. Most of the recent reports contain no statement concerning this point, but Rasmussen and Freedman noted no correlation between the severity of the pain and the degree of relief afforded by operation.

TABLE III. RESULTS OF SYMPATHECTOMY IN CAUSALGIA

AUTHOR	DORSAL SYMP THECTOMY				LOW. OR SYMP THECTOMY				ALL			
	NO	EXC	GOOD	POOR	NO	EXC	GOOD	POOR	NO	EXC	GOOD	POOR
Goodman et al	11	0		0	3	1	1	0	13	10	3	0
Kirklin et al	27	24	9	0	15	9	8	1	48	33	14	1
Rasmussen & Freedman	26	26	7	3	5	2	3	0	41	28	10	3
Mayfield & Devine	6	0	0	0	6	6	0	0	12	12	0	0
Chenoweth & Mayfield	30	30	0	0	7	26	0	0	56	56	0	0
Albritten & Maltby	8	5		1	22	6	15	1	30	11	17	
Rasmussen et al	34	31	2	1	23	15	3	0	57	46	10	1
Total	135	131	22	5	99	65	3	2	237	196	54	7

Some interesting aspects of the problem have been raised by recent observations. According to Rasmussen and Freedman the results of treatment in causalgia of the upper extremity were better when a preganglionic rather than a postganglionic operation was carried out. Albritten and Maltby and Ulmer and Mayfield have had experiences suggesting that it is desirable and sometimes necessary to sympathetomize the area of injury as well as the area to which the pain is referred. The former had a patient with a popliteal wound who was not relieved by third and fourth lumbar ganglionectomy but obtained complete relief after excision of the first and second ganglia. The latter had 3 patients with wounds of the buttocks who failed to improve after second, third and fourth lumbar ganglionectomy but had no pain after excision of the first. Two others were not relieved by first, second, third, and fourth lumbar ganglionectomy but were subsequently cured by removal of the eleventh and twelfth dorsal ganglia. Kirklin, Chenoweth, and Murphy have questioned the interpretation of these results, feeling that it is fanciful to suppose that a few failures are dependent upon inadequate extent of sympathetomy when the majority of patients with wounds of the thighs and buttocks are cured without excision of

of the nerve must be excised and the nerve sutured, or the nerve must be injected with alcohol above the level of the lesion. If local operation fails to give relief, section of the posterior roots or the opposite spino-thalamic tract in the spinal cord must be considered, but these measures will often prove ineffective. The only reference to sympathectomy is the following, contained in a discussion of median nerve causalgia. Of late dorsal sympathectomy has been advocated for causalgia.

I have cited these recommendations in no criticism of the authors. Most of the extensive experience with sympathetic interruption in the treatment of causalgia has been only recently reported. So many methods of treatment, subsequently proved ineffective had been originally reported as successful that these authors may have been justified in overlooking the early case reports of relief from sympathectomy. I have felt, however that the recommendation of often ineffectual and sometimes harmful measures in texts widely consulted by students and practitioners emphasizes the need for better understanding and broader appreciation of more reliable methods of treatment.

I do not know for certain who first utilized sympathetic interruption in causalgia. In 1907 after speaking of the good results which he had obtained during the preceding ten years with periarterial sympathectomy and excision of thrombosed vessels, Leriche<sup>24</sup> said, "In case of failure or of very diffuse pain, section of the rami communicantes would be indicated. I have never had occasion to do this. But I have operated in this fashion, as I am going to mention, in painful syndromes very like causalgia, and cure has been obtained. I believe that one will thus avoid having to resort to more mutilating rhizotomies and cordotomies." In 1929 Petit Dutaillies, Blamontier and Peron<sup>25</sup> reported a patient with apparently atypical causalgia whom they treated first by sectioning all the rami between the lower border of the superior cervical and the first thoracic ganglia. There was temporary relief after this procedure and after periarterial sympathectomy which they next carried out. Finally they excised the middle and divided the ramus to the lower three-fourths of the superior cervical ganglion. Though the patient had residual hyperesthesia of the face and ear the original pain was relieved. In 1930 appeared Spurling's<sup>26</sup> clear-cut report of complete relief of pain following excision of the second dorsal ganglion and division of the ramus to the first dorsal and stellate ganglia. Other cases were reported from time to time; for example, Kwan's<sup>27</sup> case in which the stellate and second dorsal ganglia were excised. Cases such as this one emphasized the real value of sympathectomy for the patient had previously undergone without any relief, a neurolysis, a brachial periarterial sympathectomy and then a further neurolysis with excision of an obliterated scurred axillary artery.

It is only within the past few years, however that the results of large series of cases treated by sympathectomy are available for analysis. In Table III I have summarized data concerning 257 patients recently treated in this manner. I have attempted to divide the cases into those with excellent, good and poor results. When the relief of pain has been described as complete or when only trivial pain persisted, or when the author has listed the result of operation as affording relief without qualification, I have considered the result to be

There is general agreement concerning the efficacy of sympathectomy in the treatment of causalgia. There is, however, considerable disagreement concerning the usefulness of procaine blocks as a therapeutic measure. Ulmer and Mayfield state that none of their patients obtained complete and permanent relief from blocks alone. Albritten and Maltby had two patients who were permanently relieved by a single procaine block but in their experience repeated blocks usually did not produce permanent relief. Kirklin, Chenoweth, and Murphy stated that infrequently a series of blocks relieved the pain to such an extent that no operative interference was necessary but that usually no lasting effect was noted. On the other hand, Rasmussen and Freedman obtained satisfactory results with blocks alone in 45 of 91 patients treated. In 13 of these patients the results obtained were excellent and in 32 the result was good. In none of them was further treatment required. My associates and I obtained excellent results in 1 case from one or more procaine blocks. I am thoroughly convinced that certain individuals can be treated satisfactorily by blocks alone. Our experience with sympathetic anesthesia therapy in causalgia is similar to that which I and others have had with other conditions sometimes amenable to sympathetic blocks. If the initial block gives relief for an interval of time prolonged beyond the period of sympathetic anesthesia or if repeated blocks result in relief for successively longer periods of time, one should be encouraged to continue such treatment. If the initial block, on the other hand, gives relief limited to the period of sympathetic anesthesia or more particularly if successive blocks give relief for the same or diminishing periods, one should abandon these measures and proceed with operation.

There is every evidence that the good results from sympathetic blocks and sympathectomy are the result of transient or permanent interruption of sympathetic innervation and not of some nonspecific suggestive mechanism. I have never seen pain disappear during the course of a sympathetic injection before the needle tip was introduced into the neighborhood of the sympathetic chain. Relief of pain occurred only after this area was infiltrated with procaine. Pain was not relieved in the case of the few injections which were ineffectual in producing sympathetic anesthesia. Ulmer and Mayfield had patients in whom they did not obtain the desired denervation of the upper extremity because of inadvertent removal of the fourth rib instead of the third and decentralization of the third and fourth instead of the second and third ganglia. In these patients pain was not relieved. Kirklin, Chenoweth and Murphy described some of their patients as having had incomplete denervation of the extremity according to skin resistance tests, and stated that they noted no difference in the therapeutic result in the palle is completely and incompletely denervated. These observations are somewhat puzzling to me. I have studied many patients by skin resistance and sweating tests after dorsal or lumbar sympathectomy carried out essentially as they performed them, and have always found the denervation complete according to the recognized pattern for the particular operation performed. The only exceptions have been during the transient phase of apparent sympathetic activity which is not uncommonly noted from about the fourth to the eighth postoperative day.



the first lumbar or the lower thoracic ganglia. I do not think that the two sets of observations are incompatible. We know well enough that when the first ganglion is included in a lumbar ganglionectomy the skin of the entire thigh and leg is sympathetomized according to sweating and skin resistance tests, and that only the leg and posterior surface of the thigh are denervated when the first ganglion is left intact<sup>22, 23</sup>. As yet we do not know the extent of sympathetic denervation of the deeper structures following excision of various segments of the lumbar and lower thoracic chain. Since the site of the disturbed neural mechanism which presumably initiates the pain may vary even though the skin injury is in the same location, it may be that one case is properly denervated by a less extensive operation and another only by a more complete ganglionectomy. Furthermore, there is still some question whether cure in causalgia is not effected by interruption of afferent pain fibers in the peripheral sympathetics. If such afferent fibers are present, their precise pathway is not mapped out, and although the distribution of the sympathetic efferents has been found to vary little and to follow a fairly regular pattern, any existing efferents may have a much more variable course.

I would feel that the available data suggest that at least a small number of the incomplete cures or failures following sympathectomy are explainable upon the basis of inadequate sympathetic denervation. Obviously any such cases encountered in the future should be subjected to higher sympathetic procaine blocks in order to see whether the residual pain can be relieved. Certain of the failures have occurred in cases which are almost certainly examples of atypical causalgia-like states rather than true instances of causalgia. Undoubtedly one explanation of some residual pain after operation concerns the persistence of paresthesias and mild pain of the sort commonly found in cases of peripheral nerve injury without causalgia. It is easy to understand that a patient with pain of various types should feel more acutely any remaining discomfort once the more severe and predominant pain is relieved. I have commonly observed, indeed, in cases of causalgia and in cases of peripheral neuritis undergoing subsidence of symptoms, an apparent elevation to conscious appreciation of certain paresthesias which were not complained of beforehand when a more intense pain was present. Such mechanisms undoubtedly account for certain cases of residual discomfort after sympathectomy. It is perhaps significant that these residual symptoms tend to diminish with the passage of time and often to disappear rather quickly in contrast to the course of events in most untreated cases of causalgia. It is also almost certainly true that residual pain is perpetuated in a few instances by neuropsychiatric factors. Everyone is in agreement with the original opinion of Mitchell that long-persistent severe causalgia tends to disrupt the patient's emotional balance. Cases have been observed in which it appears that persistent complaints were dependent upon psychiatric factors and in which these symptoms have subsided with reassurance. Lids and Payne<sup>24</sup> have reported one case of causalgia, perhaps atypical in certain aspects, in which psychiatric measures were the sole treatment responsible for relief of symptoms. There is not however any evidence that the pain of causalgia is primarily initiated by any psychiatric mechanism.

status of efferent sympathetic activity in these cases would offer no challenge in case of neuritis of somatic nerves we have numerous examples of relatively normal hyperactive or hypoactive motor function. There have been a number of authors who have chosen to invoke the presence of afferent pain fibers in the peripheral sympathetics in reference to the pain of causalgia and related states (Foerster<sup>13</sup> Shaw<sup>14</sup> Middleton and Bruce<sup>15</sup> Leriche<sup>16</sup>). Unfortunately no positive proof has been advanced by them.

The chief objection raised has been the lack of anatomic proof of such pathways. It is no more fanciful however to postulate their existence than to postulate without anatomic confirmation the presence of a new nociceptor set of nerves as Lewis<sup>17</sup> did in explaining certain painful states. Indeed, there are some data suggesting that such afferent nerves are demonstrable. Huntz and Farnsworth,<sup>18</sup> for example, felt that they had histological evidence of such fibers and concluded, "Any operation which effectively eliminates the vasomotor innervation of an extremity must also divide a goodly number of afferent fibers supplying the blood vessels and other sympathetically innervated tissues in the area affected." Treadgill<sup>19</sup> cited the earlier work of Dogiel as having demonstrated both motor and sensory nerve cells in the stellate ganglia of dogs.

The experiments of Burget and Livingston<sup>20</sup> and of Moore and Singleton<sup>21</sup> have been extensively quoted as demonstrating physiologically the absence of afferent sympathetic pain fibers. In these experiments a painful reaction is elicited by intra-arterial injection of an irritating solution whether or not the extremity is sympathetomized; no pain reaction follows the injection when somatic anesthesia has been produced. These experiments are clear-cut and are easily confirmed. The pain reaction does not occur however if the solution is held within a segment of the main artery but only if it is allowed to reach the terminal branches. The question naturally arises whether it constitutes a true stimulus for eliciting sympathetic pain or is merely another somatic pain stimulus having its effect once the irritant has diffused outside the vascular bed.

It is of interest that Treadgill<sup>19</sup> has recently reported experiments which suggest on the other hand that there are afferent pathways in the peripheral sympathetics. They depend upon the presence of a reaction to intense burning in an anesthetic limb with intact sympathetic innervation not present when the sympathetic chain has been excised, and upon the presence of a blood pressure response to intra-arterial injection of sodium lactate in a limb denervated by anterior and posterior root section but not elicited when the sympathetic chain has also been removed. Unfortunately experiments upon only 4 animals are reported, and further substantiation of this work is desirable before it can be accepted as proof of the existence of afferent fibers in the sympathetics.

Certain clinical observations, even though they do not offer conclusive proof, are highly suggestive of the existence of afferent pain fibers in the sympathetic nerves. For example Freeman<sup>22</sup> observed a number of paraplegic patients with pain in whom a cordotomy producing analgesia up to a level two segments higher than the site of injury failed to relieve the constant dull aching

point and setting up an abnormal state of activity in the internuncial pool in the spinal cord, and resultant initiation of abnormal motor responses from both lateral and anterior horn neurons. Relief from sympathetic interruption or from any other method of treatment is felt to result because of a breaking of the vicious circle. This clever theory invokes certain concepts which are without objective proof. Though it is ostensibly a satisfactory explanation, I feel that it leaves something to be desired. One wonders why interrupting the cycle by sympathetic block or sympathectomy is almost invariably successful and interrupting it by nerve section, careful débridement or lysis of nerves is so often unsuccessful. It is difficult to explain why the cycle cannot be broken more readily by other methods which presumably alter the state of sympathetic activity such as the production of reflex vasodilatation with apparent quiescence of sympathetic function. The question also arises as to why the effects of the internuncial pool action upon the efferents should vary so remarkably regarding the state of sympathetic activity.

Doope, Cullen and Chance explained the pain of causalgic states upon an alteration in excitability of adjacent sensory fibers by the sympathetic impulses continually at play as a result of emotional stress, the process of thermoregulation, and from various other stimuli. Though there is much to commend this theory I feel that it is challenged somewhat by the constant relief afforded by sympathetic block and the frequent lack of effect upon pain of alteration of sympathetic activity by other means. No one can deny that some efferent sympathetic impulses may be discharged rather continuously. Yet it has been generally assumed, for example, that a relative, if not complete, inhibition of sympathetic efferent impulses occurs in reflex vasodilatation. From what is known of sympathetic action one would certainly be forced to assume that sympathetic efferent activity must vary enormously with the marked changes in vascular tonus which we recognize as representing states of extreme vasoconstriction and extreme vasodilatation. According to their theory it is understandable that pain might rarely be completely relieved by any method of altering vascular tonus other than by sympathetic anesthesia or operative sympathectomy but one would assume that such maneuvers should rather regularly alter the severity of the pain. Consequently the validity of the theory is brought into question by the failure of such methods to influence the pain at all in many cases. Doope, Cullen, and Chance, Rasmussen and Freedman, Harter<sup>11</sup> and I have studied cases of causalgia and of other allied painful states in which extreme vasoconstriction induced by such measures as local cooling, general body cooling subcutaneously or even intra-arterially administered airenalia have not altered the pain. Extreme vasodilatation induced by such measures as local heat, reflex vasodilatation, reactive hyperemia, and Prostigmin given intra-arterially have failed to affect the pain in any appreciable way. Yet sympathetic block has brought about prompt and complete relief in these same cases.

Obviously assumption of the existence of afferent pathways in the peripheral sympathetics would enable one to explain the pain of causalgia and its relief by sympathetic interruption in a most satisfactory manner. The variable

which in retrospect would have been informative. It is unlikely that an opportunity will again present itself for study of such large groups of cases. It is entirely possible, however, that intensive study of fewer cases may settle some of the remaining problems.

It would seem important to study the vasomotor responses in each patient by every available method, including digital plethymography and venous occlusion plethymographic blood flow methods whenever possible. It will be profitable to pursue further the reaction of patients to alterations in the state of vascular tonus induced by various methods, and to study the effect of a variety of drugs affecting autonomic function, including such agents as tetraethylammonium chloride. It will be important to correlate better the time of onset of vasodilatation and of pain relief following sympathetic block, and to evaluate carefully any persistence of pain during spinal anesthesia. Particular study must be made of cases of incomplete relief of pain after sympathectomy. The so-called atypical causalgias require further clarification. Finally it is hoped that more animal experimentation may throw new light upon the problem of the nerve pathways and the mechanism of pain. Better understanding of the fundamental problems connected with major causalgia may be of aid in understanding more clearly the other allied painful states.

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sympathetic

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or burning pain, though the intermittent types of pain had ceased; these same patients were completely free of pain after a cordotomy performed at the second dorsal level. Operations which gave levels of analgesia at any point below the fourth thoracic dermatome often failed to relieve burning pain but all pain was relieved if the level was at or above the third dorsal dermatome. Since this type of pain was not affected by operations which severed the central pathways of the somatic pain fibers from the entire area in which the pain was felt and from the area of injury but was cured by a higher cordotomy he felt that the most plausible explanation lay in the transmission of the pain impulses through fibers in the sympathetic nerves entering the cord at a high level. I have already referred to other suggestive clinical observations. Still other personal observations I present apologetically since they are inadequately controlled, but I do so in the hope that they may stimulate similar but better controlled, observations. I have treated several patients with severe causalgia in whom complete relief of pain occurred promptly after procaine infiltration in the region of the sympathetic chain some time before thermocouple readings revealed any rise in skin temperature. This occurrence reminds one of the sensory anesthesia which so often precedes motor paralysis in spinal anesthesia or somatic nerve block. One cannot assume, however, that efferent sympathetic paralysis occurred after subsidence of pain at the time the increase in skin temperature was first noted. Vasodilatation may have preceded the rise in skin temperature and may have occurred simultaneously with cessation of pain. Constant digital plethysmographic tracings as well as skin temperature and skin resistance measurements in such cases should settle the matter one way or the other. I have treated a few patients in whom the causalgic pain was not relieved by spinal anesthesia which was adequate for comfortable exposure of the lumbar sympathetic chain and for full vasodilatation of the lower extremities; in these same patients the pain ceased promptly with excision of the sympathetic chain. Such observations are highly suggestive of the existence of afferent pain fibers in the sympathetic nerves. Unfortunately only a few such observations were made and in none of them was the precise level of anesthesia carefully checked, though the level must have been as high as the seventh dorsal segment since there was no pain in the operative incision.

It may be concluded that none of the current theories of the mechanism of pain is entirely satisfactory and that further intensive study is required.

#### SUMMARY

I have reviewed the early and recent contributions to the problem of causalgia and have attempted to discuss the signs and symptoms, the motor status, the treatment, and the mechanism of pain. Much of the broad experience with this disorder was obtained only recently as a consequence of World War II. Though every effort was made to segregate such cases in special centers where the best opportunity existed for their careful evaluation and treatment, it is nevertheless true that the enormous volume of work, the limited personnel, and the lack of availability of certain apparatus precluded particular studies

# EXPERIMENTAL CARDIAC HYPERTROPHY

## THE ACUTE EFFECT OF PULMONIC AND AORTIC STENOSIS

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CARDIAC hypertrophy has been studied experimentally by the reproduction of various cardiovascular lesions which are known, in clinical medicine, to be associated with enlargement and hypertrophy of the heart. Aortic regurgitation may be produced by cutting an aortic cusp with a valvulotome passed through the carotid artery or left ventricle. As a result of this lesion, general cardiac hypertrophy developed, the most marked effect being in the left ventricle<sup>1,2</sup>. An experimental interventricular septal defect produced by piercing the septum with a knife valvulotome introduced through the left ventricle resulted in hypertrophy of both ventricles. Similar results were obtained with arteriovenous fistulas, and in this lesion hypertrophy was shown to be reversible by repair of the fistula<sup>3</sup>. The left ventricle will hypertrophy in response to the stimulus of experimental hypertension, and experimental hyperthyroidism will cause hypertrophy of both ventricles. Constriction of the pulmonary artery or the aorta led to hypertrophy of the ventricle affected by the experimental stenosis.

The most important factor producing hypertrophy of the heart is increased work, which is brought about in these experimental lesions either by increased pressure in the affected ventricle (hypertension, valvular stenosis) or by the effort necessary to propel an increased volume of blood (valvular insufficiency, septal defects, arteriovenous or arteriopulmonary connections). Though the broad relationship between increased cardiac work and hypertrophy is generally though not unanimously accepted, many questions in connection with this problem still remain unanswered.

Thus, the rate of hypertrophy of cardiac muscle has attracted little attention. Stewart was able to recognize some hypertrophy one week after the production of an experimental lesion, while Herrmann, using similar methods, concluded that weeks or months elapsed before definite hypertrophy developed.

The purpose of this study was to investigate the rapidity of hypertrophy of cardiac muscle in response to an adequate stimulus and to determine whether under these circumstances hypertrophy is a continuous process, extending over a long period of time. During the study a satisfactory method of producing acute pulmonic or aortic stenosis was developed. This and a few convincing results justify a report at this time.

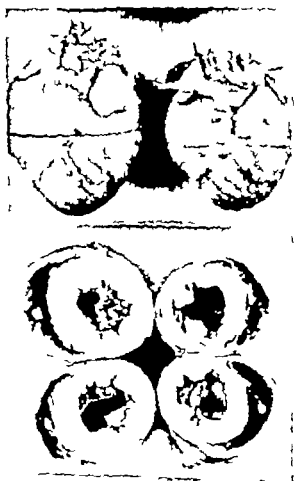
### TECHNIQUE

Stenosis of the proximal aorta or pulmonary artery can be produced by several methods. A broad cotton or silk ligature may be applied tightly

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adequately without erosion of the vessel wall (Fig. 1). A frequent complication resulting from an acute constriction of the aorta or pulmonary artery is heart failure resulting from too rapid increase in intraventricular pressure. This difficulty was partially overcome by the gradual production of the stenosis, in several stages, at ten minute intervals. Animals then survived with a higher degree of stenosis, and the mortality from heart failure dropped considerably.



#3

CONTROL

Fig. 2.—Sterile animals, three weeks. Note the gross enlargement of the heart as compared with the control. In the cross sections here the left ventricle is placed side by side to show the increased thickness of the ventricular wall in the animal operated upon.

## METHOD

The dogs were anesthetized with intravenous nembutal. Respirations were controlled with an intratracheal tube and a mechanical respirator. Using sterile



enough to reduce the caliber of the vessel one-third to one-half. This is a relatively simple method, but frequently erosion of the vessel wall occurs, resulting in fatal hemorrhage. The same objection is found when metallic bands are used.<sup>4</sup> To obviate this difficulty Holman placed loose ligatures around the aorta and pulmonary artery in puppies. As the animals increased in size the

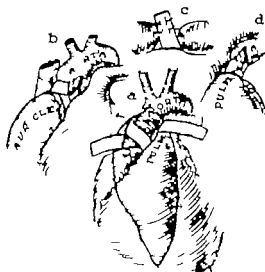


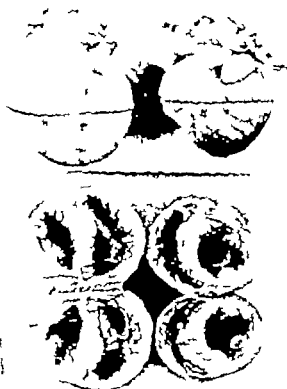
Fig. —a and b Technique of producing aortic stenosis with preserved fascia lata side view  
c, pulmonary stenosis.

vessel remained constricted at the site of the ligature, resulting in a gradually developing stenosis. This method, however, is not suitable for the study of the rate of growth of the cardiac muscle where an acute stenosis of a high degree is desirable. We have found that a strip of preserved fascia lata, sutured around the great vessels in a figure-of-eight manner will maintain the stenosis.

TABLE I. AORTIC AND PULMONARY STENOSIS (THREE WEEKS OLD PUP)

EXPERIMENTAL NO.	VESSEL STENOSED	BODY WEIGHT IN GRAMS AT EXCISION	HEART WEIGHT IN GRAMS AT EXCISION	PROPORTION HW TO BW	BODY RESP.		MEAN TENSION OF VENTRICLE IN MM.
					AT STENOSIS	BELOW STENOSIS	
8 female (9 mo old) Control female Latter mate	Aort	6240	70	0.011	13	28	10 (Left)
		6200	46	0.074		25	7 (Left)
17 male (3 mo old) Control female Latter mate	Aort	3110	5	0.0016	3	35	8 (Left)
		100	23	0.234		28	6 (Left)
15 male (3 mo old) Control male Latter mate	Pulmonary artery	4150	43	0.0104	15	44	6 (Right)
		4200	27	0.0065		4	4 (Right)

malis, and pulmonary stenosis in one. It was thought that the heart weight to body weight ratio, as determined by Herrmann, could be used as a standard control for these experiments. His studies of 700 dog hearts revealed a mean heart weight/body weight ratio of 00.98 with a minimum of 00.600 and a maximum of 00.994. Using Herrmann's methods for determining the heart weight/body weight ratio, we found the following values in the first seven



#13

CONTROL

Fig. 4.—Pulmonary stenosis, three weeks. The right ventricle is markedly enlarged as compared with the control. The cross sections below are shown with the right ventricle in perspective. Illustrate the increase in thickness of the ventricular wall in the animal operated upon.

experiments 0078 0080, 0083 0090 0101 and 0115. Although six of the seven ratios were above 11 mm an a mean only the last two could be accepted as indicating definite hypertrophy. These two instances occurred in an animal with pulmonary stenosis of three weeks duration and in an aortic stenosis of four weeks duration. For the most part these experiments merely indicated that acute hypertrophy was occurring in response to the stimulus of stenosis.

precautions, the heart was exposed by resecting the third or fourth rib and the pericardium was opened. Either the proximal aorta or pulmonary artery was separated from its adjacent structures, and the fascial band was placed around the vessel. After gradually tightening it for about forty minutes, several sutures were placed to hold the degree of stenosis created. The pericardium was approximated loosely with a few interrupted sutures, the lung was inflated and the chest was closed in layers. The animals were sacrificed after varying time

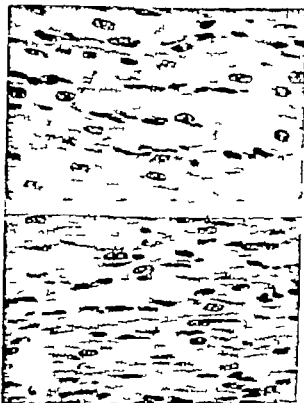


Fig. 3.—Microphotographs of the left ventricle in Experiment 5 (upper) as aortic stenosis of three weeks duration, as compared with its control (lower). Note the marked increase in the cytoplasm of the muscle fibers causing separation of the nuclei.

intervals. The body weight at necropsy was recorded, the heart removed, and the degree of stenosis and the caliber of the vessel just beyond the stenosis were measured with bougies. After trimming away the pericardium, excess fat and great vessels, the heart were washed free of blood, emptied, and weighed. They were then fixed in formalin for one week, and thereafter cut transversely at similar levels, so that the thickness of the wall could be measured. Microscopic slides were made from like areas in the experimental and control animals.

#### RESULTS

In the first seven experiments adult dogs were used, being sacrificed after a period of one to four weeks. Aortic stenosis was produced in six of these and

the time factor. It was felt that the only reliable criterion of cardiac hypertrophy is the increase in muscle mass, and other evidence such as roentgenographic appearance, measurements of the heart and thickness of the heart wall, though recorded, were considered as only secondary. In order to simplify the problem the general heart weight was determined, rather than separate weights of cardiac chambers, for even the best methods of division of the heart may introduce a new error.

While the relationship between the increase in cardiac weight and the degree and duration of the stenosis will be the subject of a detailed study one fact has been established. It was shown that with an adequate stimulus, definite hypertrophy develops within three weeks. The degree of hypertrophy which in Experiment 10 amounted to a 65 per cent increase over the control animal is comparable to the results of Holman, Hermann, and others whose experiments extended over a period of many months. This would indicate that hypertrophy of the heart can be an acute process with most of the growth occurring within a short time after the stimulus of hypertrophy is established.

## SUMMARY

A method of producing experimental aortic and pulmonary stenosis is described which enabled us to establish a high degree of stenosis with a low mortality. It was shown that pulmonary or aortic stenosis causes definite hypertrophy of the right or left ventricle within three weeks, the degree of which is comparable with the hypertrophy found in experimental stenosis of many months duration.

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It was realized that a more accurate measure of the degree of hypertrophy could be obtained if carefully matched litter mates were used, retaining one animal as a control.

Seven experiments were performed on litter mates, all of them young animals. In six of these aortic stenosis was created and in one pulmonary stenosis. Two sets of animals were sacrificed after one week, one after two weeks, and four after three weeks. In four experiments no definite hypertrophy was

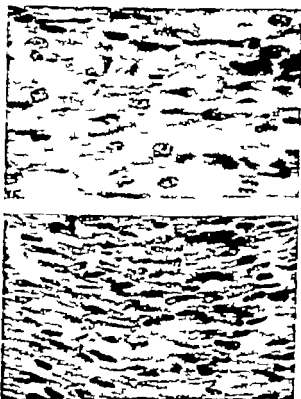


Fig. 5.—Microphotograph of section of the right ventricle in Experiment 13 (upper) pulmonary stenosis of three weeks' duration compared with its control (lower) but the enlarged muscle fibers in the animal operated upon.

found, and in all of these the stenosis was found to be very slight. Three experiments, all of them in the three week group were successful, and showed marked cardiac hypertrophy. The results are presented in Table I. Fig. 2 shows the gross specimen of Experiment 8 (aortic stenosis) with the litter mate control. Fig. 3 shows the microscopic section of the left ventricle clearly indicating hypertrophy of the muscle fibers, compared with the control animal. Figs. 4 and 5 present the gross findings and a microphotograph of a section of the right ventricle in the case of pulmonary stenosis, and the control

#### DISCUSSION

In our experimental study of cardiac hypertrophy there were two variables: the degree of stenosis, acting as stimulus of cardiac hypertrophy and



# THE RELATIONSHIP BETWEEN GROSS TYPE OF GASTRIC CARCINOMA AND ANACIDITY

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WHILE most patients with gastric carcinoma have achlorhydria at the time the diagnosis is established, a significant number have free acid in at least some degree. It seemed worth while to determine whether in our material, the presence or absence of achlorhydria bears any constant relationship to the gross type of carcinoma and whether among patients with free acid, there is any unusual deviation from normal ranges of acidity in relation to any type of carcinoma. With reference to these points the results of a review of 284 cases in which gastric resection was performed are presented.

## MATERIAL

For this study we have selected, from among those cases in which gastric resection had been performed, all cases in which both gastric acidity had been determined and the resected specimen was available for re-examination. The data to follow concern 284 such cases.

The carcinomas were classified according to the method of Borrmann: Type I polypoid carcinoma; Type II sharply demarcated, ulcerating carcinoma; Type III partly sharply demarcated, partly infiltrating carcinoma; Type IV diffusely infiltrating carcinoma. This classification is convenient to use but has no special advantages over other and as with any classification, one must sometimes be arbitrary as to the designation of a given tumor. The classification makes no distinctions on the basis of size of a tumor. Thus a Type IV tumor might be apparently limited to small area or might obviously infiltrate the whole stomach.

The acid determinations varied as to method. Although a fractional analysis after histamine stimulation had been employed for the great majority, alcohol had been used in some cases and, in a few, only fasting samples had been analyzed. In all cases the highest recorded value for free acid was noted and those cases where free acid was present were further subdivided according to whether the values exceeded or were less than 20 degrees. Those cases in which the record clearly showed that histamine had been employed as the test substance were also considered separately. This maneuver eliminated some cases in which there was free acid on fasting samples and also eliminated others in which though histamine had been undoubtedly employed, the fact was not clearly shown in the record. The results of consideration of this restricted group, 239 cases, are, however, comparable to those of the entire group.

## PRESENTATION OF DATA

These data appear in the accompanying tables where acidities are considered with reference to age, sex, and gross type of carcinoma. Table I shows the dis-

TABLE I. RELATION OF TUMOR TO ACID SECRETION IN 40 SOL MASSES

AGE (YR.)	TYPE I				TYPE II				TYPE III				TYPE IV				ALL CASES			
	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID
34-40	1	1	1	2	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
41-50	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
51-60	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
61-70	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
71-83	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
Total	5	5	5	15	5	5	5	15	5	5	5	15	5	5	5	15	5	5	5	15

TABLE II. RELATION OF GROSS TYPE OF TUMOR TO ACID SECRETION AMONG 75 SOL MASSES

AGE (YR.)	TYPE I				TYPE II				TYPE III				TYPE IV				ALL CASES			
	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID	MEASUREMENT	REL. ACID LESS THAN 20	REL. ACID MORE THAN 20	TOTAL WITH REL. ACID
34-40	1	1	1	2	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
41-50	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
51-60	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
61-70	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
71-81	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3	1	1	1	3
Total	5	5	5	15	5	5	5	15	5	5	5	15	5	5	5	15	5	5	5	15





tribution of the four types of tumor and the corresponding acidities according to age among 705 men. Table II shows the same data for 9 women. Table III combines the two sexes. Table IV shows the composite data for the 239 cases in which histamine had clearly been used as a test substance.

Examination of the tables reveals no real difference dependent on either age or sex and the incidences of an acidity are of comparable magnitude for the two sets of data relative to all acid determinations and those with verified histamine stimulation alone (Tables III and IV). The results can be conveniently summarized in terms of Table III which includes all cases.

Of the 284 cases, 165 (58 per cent) showed achlorhydria, and 99 (35 per cent) showed free acid. Of these 35 (12 per cent of the total) had maximum values of less than 20 degrees and 64 (22 per cent of the total) had maximum values of more than 20 degrees. The incidences of the acidities in each of the decades are quite comparable to that of the entire group.

There were 9 Type I tumors, all of which were associated with achlorhydria. These comprise 3 per cent of the total number and account for 5 per cent of the cases of achlorhydria.

There were 79 Type II tumors (27.8 per cent of the total) which provided for 57 (31 per cent) of the cases of achlorhydria. Twenty-two (28 per cent) of the Type II tumors were associated with free acid and thus accounted for 22 per cent of the total number of cases with free acid. Of these 9 had less and 13 had more than 20 degrees.

There were 4 Type III tumors (1.6 per cent of the total) which accounted for 31 (1 per cent) of the cases with achlorhydria. Sixteen (34 per cent) of the Type III tumors were associated with free acid (16 per cent of the total cases that showed free acid) and, of these 5 showed maximum values of less than 20 degrees and 11 showed more than 20 degrees.

There were 149 Type IV tumors (52.5 per cent of the total) and among these there were 68 (48 per cent) of the cases with achlorhydria. Sixty-one (41 per cent) of the 149 cases showed free acid (62 per cent of the total number of cases with free acid). Of these 1 had maximum values of less than 20 degrees and 40 had more than 20 degrees.

The values for the cases in which histamine was certainly employed are of the same order of magnitude (Table IV). None of the Type I tumors, 22 per cent of the Type II tumors, 79 per cent of the Type III tumors, and 4 per cent of the Type IV tumors were found to be associated with free acid. Thus, 83 per cent of this series showed free acid in at least some degree.

#### COMMENT

In this series of cases only the tumors of Type I were constantly associated with achlorhydria and these comprise but 3 per cent of the group. With each of the other types of tumor a significant proportion of the cases showed free acid and, among these, the proportion was somewhat higher for tumors of Type IV than for Types II and III. Of the cases with free acid about one third had values below 20 degrees, and two-thirds had values over 20 degrees.

This distribution is also approximated for each of the three types concerned. A further breakdown of the acidities in excess of 20 degrees show that of the 64 cases, 23 had maximum values between 20 and 30 degrees, and 41 had maximum values over 30 degrees. For the great majority of cases of gastric carcinoma there is no special relationship between achlorhydria or hypochlorhydria and a gross type of tumor.

Summarized differently in this series of 284 cases, 243 (86 per cent) had a chlorhydria or acid values below 30 degrees, 220 cases (77 per cent) had achlorhydria or acid values less than 20 degrees, and 185 cases (65 per cent) had achlorhydria. While these data follow others in showing the predominance of reduced secretory capacity as of the time the diagnosis is made, in a group of cases of gastric carcinoma they also emphasize the fact that no range of acidity precludes the disease. Emphasis on the examination of individuals with achlorhydria or hypochlorhydria in order to detect most early gastric cancer is valid, however only to the extent that achlorhydria with cancer also means achlorhydria before the cancer appears. The constancy of this relationship is established only in the case of pernicious anemia, though the study of Comfort, Halsey and Berkson showed more achlorhydria and hypochlorhydria among patients who subsequently developed cancer than was normal for the ages concerned.

The character of the mucosa in these cases is to be considered in a separate report, but it may be noted here that for many there is an anatomic basis for anaecidity as evidenced by complete loss of normal body glands. Such extensive atrophy may be found in association with tumors of any gross type, but it seems to be most consistently present with tumors of Type I. The group concerned is, of course, small but Dockerty<sup>3</sup> has called attention to a similar relationship. On the other hand, diffuse atrophy by no means necessarily accompanies gastric carcinoma (Hebbel) and other patients in this series presented well-preserved body mucosa even though achlorhydria had been demonstrated. Here, achlorhydria is less readily explained. That histamine achlorhydria is not necessarily permanent is well known and perhaps, were repeated analyses to be performed, free acid might at some time be present in some such cases. Magnus<sup>4</sup> found no gastritis in the body mucosa in 22 of 26 cases of ulcerating carcinoma, and expressed the opinion that if achlorhydria precedes gastric carcinoma it is not due to the loss of parietal cells.

#### SUMMARY

In a series of 284 cases of gastric carcinoma, 43 (86 per cent) had achlorhydria or maximum acid values below 30 degrees, 220 cases (77 per cent) had achlorhydria or maximum acid values below 20 degrees, and 185 cases (65 per cent) had achlorhydria. Achlorhydria was uniformly present only in association with tumors of Borrmann Type I and these totaled but 9 per cent of the series. For tumors of Borrmann Types II, III and IV there was no constant association of either achlorhydria or hypochlorhydria. Twenty-eight per cent of the Type II tumors, 34 per cent of the Type III tumors, and 41 per

cent of the Type IV tumors were associated with free acid on gastric analysis. In each of these groups the maximum acid values fell below 20 degrees in about one third of the cases and exceeded 20 degrees in about two-thirds of the cases.

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cent of the Type IV tumors were associated with free acid on gastric analysis. In each of these groups the maximum acid values fell below 20 degrees in about one-third of the cases and exceeded 20 degrees in about two-thirds of the cases.

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# CLINICAL STUDIES IN CRANIOSYNOSTOSIS

## ANALYSIS OF FIFTY CASES AND DESCRIPTION OF A METHOD OF SURGICAL TREATMENT

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### INTRODUCTION

THE striking and often grotesque deformities associated with premature closure of the cranial sutures have interested both physicians and laymen since antiquity. Descriptive names of Greek derivation, such as scaphocephaly, acrocephaly, turriccephaly, and oxycephaly, were used to designate these bizarre abnormalities of the head. With discovery of the roentgen ray a more accurate clinical terminology based on physiologic and pathologic criteria became possible. Searl and others, therefore, have recommended adoption of the term *craniosynostosis* to include all varieties of premature closure of the cranial sutures, adding to this diagnosis identification of the particular sutures involved in each instance. This terminology will be used in the present report.

The cranial sutures normally fuse long after the growth of the brain has been completed. Only the metopic suture normally closes at birth or shortly thereafter; the others remaining open until the age of 50 or 60 years. Boileau has differentiated two phases in the surface growth of the cranial bones in infants. In the first phase, which extends into the second year of life, growth at the border of the membranous bones predominates. At the beginning of the second phase, the sutures become densified and diffuse growth of the bones takes place at a slower rate. Extreme abnormality probably occurs only when synostosis begins during fetal life or shortly after birth, but lesser degrees of deformity are commonly seen when synostosis occurs within the first two years.

Craniosynostosis has been almost attributed to syphilis, rickets, prenatal or birth trauma, endocrine disorders, and meningitis. There is little foundation for any of these theories and reviewing them would be of historical interest only. Patterson in an unpublished review of Cushing's cases of *synostosis cranii* emphasized three important points: an inherent mesenchymal defect as the cause of premature closure of the sutures; first, there is a strong hereditary tendency; cases having been reported in two generations; and several cases having occurred in siblings; second, associated congenital anomalies, particularly syndactylism, are commonly seen; and third, there is a greater incidence in males (80 per cent) than females.

Many anatomic investigations of skull show germinal synostosis has been made notable among which is the detailed study of acrocephaly by Greig. Histologic studies through the suture lines and of the supra-membranous bones of the skull have revealed nothing remarkable. The lack of a normal

microscopic abnormality in the bone itself has been confirmed by examination of many specimens removed at operation in the series of cases reported here. Likewise there is no evidence that the actual growth and repair of membranous bone in these patients are impaired. In fact, it would appear that healing of bone occurs more rapidly in these patients than in normal patients.

A variety of apparently unrelated congenital anomalies has been described in association with premature closure of the cranial sutures. Park and Powers reviewed twenty-eight cases of so-called acrocephaly in which there were varying degrees of syndactylism, a syndrome which has been termed acrocephalo-syndactylism. Other anomalies including cleft palate, harelip, congenital heart disease, spina bifida, and meningocele have been reported in association with craniosynostosis. Such anomalies apparently occur more frequently with this condition than in normal individuals.

Although the bony abnormalities in craniosynostosis are important, because of the grossly deformed heads which may result of much greater significance is the compression of the growing brain which occurs secondary to this premature bony fusion. The relation of premature closure of the cranial sutures to mental development has often been misinterpreted, principally because of confusion of this condition with true microcephaly. Because of the vast difference in treatment and in prognosis, the fundamental difference between these conditions should be clearly understood. In microcephaly the primary difficulty is failure of the brain to grow. The cranial sutures are present but the head does not expand because there is no growth pressure from within. In craniosynostosis growth of the brain is normal, except as it is restricted by the limitations of the prematurely fused cranial sutures. In microcephaly decompressive procedures are of no avail in the prevention or treatment of cerebral deficiency. In craniosynostosis on the contrary early prophylactic decompression which permits expansion of the brain to approximate a normal rate should allow mental development to proceed unhindered.

Scammon and Dunn and Coppoletta and Wolbach have determined that the brain increases about 85 per cent in weight in the first six months and 130 per cent in the first year of life (Fig. 1). After the second year growth is slower but still rapid and after the eighth year relatively little increase in brain bulk occurs.

The clinical implication of these observations is readily apparent, namely, the earlier the onset of premature craniosynostosis, the more likely is damage to ensue. Conversely, the earlier premature closure of the sutures is recognized and alleviated by surgical treatment, the less likelihood there is of subsequent cerebral deficiency.

Faber and Towne were the first to stress the importance of early surgical treatment to prevent mental retardation and visual impairment. The purpose of the present report is twofold: first of all to present clinical studies of fifty cases of premature craniosynostosis seen at the Children's Hospital and to re-emphasize the importance of diagnosis and treatment in the first months



of life, and second, to describe a method of surgical treatment in this age group. The historical development of therapy for premature craniosynostosis, as well as the signs, symptoms, classification, roentgenologic findings, and the diagnosis have been reviewed recently by Simmons and Peyton and will be discussed here only in brief.

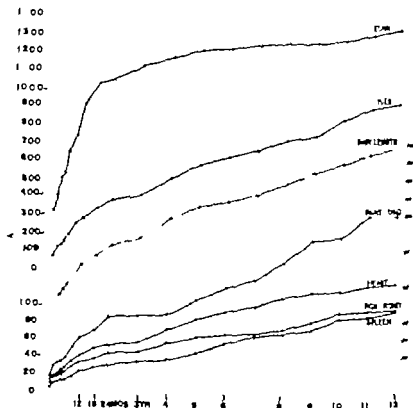


Fig. 1.—Chart showing rapid increase in brain weight in first two years compared to other organs of the body. (Growth of the brain is much slower after two years. After Osipovitch and Wolfshub. *Am. J. Path.* 1923.)

#### ANALYSIS OF CASES

Virehow<sup>16</sup> recognized that when one or more of the cranial sutures closes before the rapid growth of the brain is completed, the skull expands in a direction axial to the closed suture. Thus when the sagittal suture closes prematurely the coronal and lambdoid sutures permit greater anteroposterior expansion than would normally occur. The skull therefore, becomes elongated or scaphocephalic. Similarly if the coronal suture alone closes prematurely the patent sagittal and squamosal sutures permit added lateral growth and the forehead becomes prominent and wide or acrocephalic. When closure of the coronal, sagittal, and lambdoid sutures occurs prematurely the head can

expand only upward at the anterior fontanel. To this type of deformity the term oxycephaly has commonly been given. The base of the skull becomes deepened, the sinuses obliterated and the orbits shallow. The head is small and narrow at its vertex. There may also be synostosis between the facial bones resulting in severe distortion of the face.

The cases in the present series fall into four main groups: (1) those in which the sagittal suture alone is closed; (2) those in which the coronal suture has closed; (3) those in which two sutures have closed; and (4) those in which all of the sutures have closed. The clinical picture and course, the prognosis, and the operative treatment are in each group although the fundamental pathology is the same. Rarer miscellaneous types of craniosynostosis will be mentioned briefly after considering each of the four main groups separately.

*Premature Closure of Sagittal Suture*—In the present series, there have been twenty-nine cases of premature closure of the sagittal suture. Of these twenty-four were in males and five in females. Of the twenty-nine a total of nine cases have been found with associated congenital anomalies. These included an ectopic right kidney, congenital hypertrophic pyloric stenosis, a cecum *sepi pellucida* shown in a pneumoencephalogram, a hemangioma of the thigh, a mild hypoplasia, a cholesteatoma of the skull, a congenital dislocation of the cervical spine as well as clubhands and clubfeet, webbed toes, syndactylism of both hands and feet and cartilaginous inclusions of both humeri.

There were seven definitely retarded children. One of these, a girl, was operated upon at the age of 8 months. A pneumoencephalogram showed marked atrophy of the cerebral cortex. Right subtemporal decompression and parasagittal craniectomies failed to bring about any improvement and the patient showed, at the age of 3 years, 8 months, evidence of severe retardation. Five of the other children showing evidence of retardation before operation have presented a slightly more optimistic picture. They were first operated upon at 1 month, 19 months, 24 months, 35 months, and 5 years, respectively. In three of this group there was felt to be definite improvement after operation, though evidence of retardation persisted. The fourth has been followed for too short an interval to permit reliable observation; one patient was not operated upon.

Ocular difficulties have rarely been seen associated with premature closure of the sagittal suture. One patient showed mild exophthalmos without apparent disturbance in vision; another patient treated at the age of 1 year by bilateral subtemporal decompression was reported to have diminution of vision in one eye and a marked strabismus.

Four patients in this group have had pneumoencephalograms. In one there was evidence of severe cerebral degeneration which it was felt occurred coincidentally with synostosis rather than as a result of it. In the other three cases, the question of mental retardation was raised and pneumoencephalograms were done to aid in evaluation. In each instance the deviation from normal in the pneumoencephalogram was light. One of these children, who

of life, and second, to describe a method of surgical treatment in this age group. The historical development of therapy for premature craniosynostosis, as well as the signs, symptoms, classification, roentgenologic findings, and the diagnosis have been reviewed recently by Simon and Perion and will be discussed here only in brief.

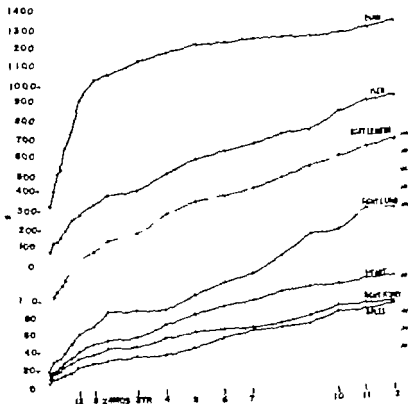


FIG. 1.—Chart showing rapid increase in brain weight in first two years compared to other organs of the body. Growth of the brain is much slower after two years. (See Perion, Cerebrolectia and Wolffish, *Am. J. Path.* 1933 '7)

#### ANALYSIS OF CASES

Virchow<sup>22</sup> recognized that when one or more of the cranial sutures closes before the rapid growth of the brain is completed, the skull expands in a direction axial to the closed suture. Thus when the sagittal suture closes prematurely the coronal and lambdoid sutures permit greater anteroposterior expansion than would normally occur. The skull, therefore, becomes elongated, or scaphocephalic. Similarly if the coronal suture alone closes prematurely the patent sagittal and squamosal sutures permit added lateral growth and the forehead becomes prominent and wide or acrocephalic. When closure of the coronal, sagittal, and lambdoid sutures occurs prematurely the head can

Patients who present the characteristic deformity at birth of scaphocephaly and are operated upon in the first few weeks of life show a striking change in contour of the head (Fig 4). Patients operated upon after the age of 10 to 12 months are less likely to show change in skull contour but frequently show more marked clinical improvement since the cerebral hemispheres of these children have undergone deformity over a longer period of time. Children operated upon after the age of 2 years show little immediate



Fig 4 (Case 2).—A and B, Upper photographs show patient as an infant before operation at which time she was considered to be retarded. She was operated upon soon after this photograph was taken. C and D, Lower photographs show patient at the age of 12 years.

alteration in skull shape but again the clinical improvement may be impressive. A striking example of alteration of the shape of the cranial cavity is evident in the illustration of Case 23 (Fig 5). The deformity of the infant's head was noticed at birth, the diagnosis confirmed by roentgenography within the first two weeks, and the patient operated upon at the age of 5 months. The postoperative photographs taken at the age of seven months show the striking change toward normal.

showed slight dilatation of one lateral ventricle has been followed to the age of 15 years and is on the honor roll in school. The other two children who showed slight ventricular dilatation are now normal or only slightly retarded.



A

B

C

Fig. 2 (Case 9)—A, B, and C. Premature closure of sagittal suture; the head is elongated and narrow.



Fig. 3 (Case 5)—Brother of another patient (Case 39). These siblings showed premature closure of sagittal suture at birth. This patient, the older brother, was operated on as an infant. He is now at the age of 15 years, normal in every respect.

Fifty-five per cent of the patients have been operated upon in the first year of life. Of the last eleven all of whom have come to the Neurosurgical Clinic in the past year only four have been over 1 year of age. All were under 9 years (Figs. 2 and 3).

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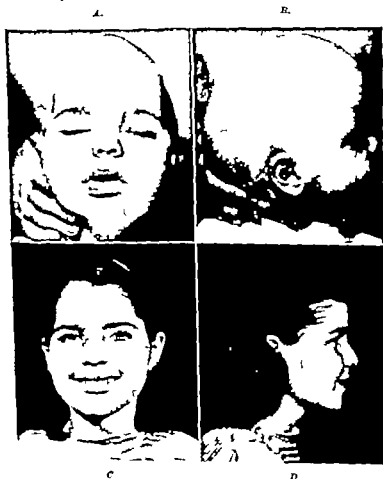


Fig. 4 (Case 3)—A and B, Upper photographs of new patient as infant before operation at which she was considered to be retarded. She was operated upon soon after the photograph was taken. C and D, Lower photographs show patient at the age of 12 years.

alteration in skull shape but again the clinical improvement may be impressive. A striking example of alteration of the shape of the cranial cavity is evident in the illustration of Case 23 (Fig. 5). The deformity of the infant's head was noticed at birth, the diagnosis confirmed by roentgenography within the first six weeks, and the patient operated upon at the age of 5 months. The postoperative photographs taken at the age of seven months show the striking change toward normal.

Of the twenty nine cases in this group, twenty-seven patients have been operated upon. Since 1835 several types of operations have been used, including subtemporal decompressions and multiple linear craniectomies. Bilateral parasagittal craniectomy has proved to be the operation of choice for premature closure of the sagittal suture. Mount<sup>11</sup> has performed a

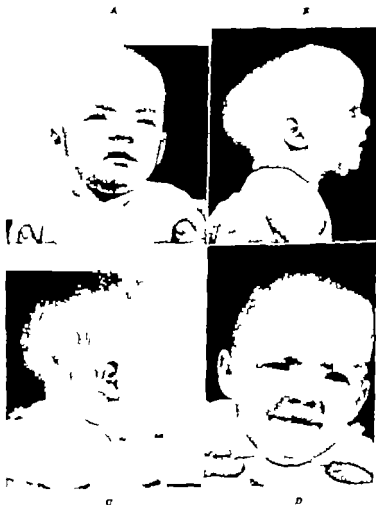


Fig. 8. (Case 23).—A, B, C, and D. Pre- and postoperative photographs of patient with premature closure of sagittal suture. Postoperative photographs show normal contour of head two and one-half months after bilateral parasagittal craniectomy performed at the age of 3 months.

midline sagittal craniectomy in cases of this type but such a procedure endangers the sagittal sinus, both at the time of operation and during the postoperative period. In this series a strip of bone in the midline has been left for the protection of the sinus.

An illustrative case from this group is outlined here.

**CASE REPORT**—C. E. D. (Fig. 6) was first admitted to The Children's Hospital with right upper lobe pneumonia at the age of 9 months. At that time the anterior and posterior fontanelles were closed and the head was deformed with prominence of the frontal region. Roentgenographic examination of the skull at the age of 15 months showed the sagittal suture to be fused. The patient developed normally to the age of 4 years and was not referred for surgical treatment. Between the ages of 4 and 6 years he became very irritable and uncooperative. He constituted a distinct behavior problem in his home and developed enuresis, symptoms he had not displayed previously.

In July 1938 he was referred to the Neurosurgical Clinic. He was well developed and nourished boy who was very uncooperative. Complete physical and neurological examinations were normal. There was no papilloedema. Laboratory studies of blood and urine showed no abnormalities. A pneumoencephalogram showed moderate dilatation of the left lateral ventricle and no other abnormalities.



Fig. 6. Case 1: A and B Roentgenograms of patient, aged 6 years, with craniosyneustotic deformity of sutures before surgery for problem. A greatly improved by operation. He was no longer out of school at age of 11 years. Note fusion of sagittal suture and slight increase in cranial markings of skull.

Bilateral subtemporal decompressions were performed in July 1939. He was seen one month after discharge from the hospital, at which time his mother reported that she and her neighbors were amazed by his personality improvement. At the age of 11 years he was doing well in the 8th grade. He was last seen on July 15, 1946, at the age of 14 years. He showed no signs of pressure; the decompressions were still open and soft, and he was noted to be on the honor roll in school.

**Premature Closure of Coronal Suture**—Premature closure of the coronal suture alone presents a striking contrast to closure of the sagittal suture. The anterior portion of the head becomes high and broad. There is frequent gross deformity of the forehead, occasionally hypertelorism and ptosis of the eyelids. Asymmetry is commonly seen in those cases in which the closure



occurs after birth since one coronal suture may fuse completely before the other.

In the present series there were eight patients with premature closure of the coronal suture, five females and three males. Three of these children showed evidence of mental retardation to objective psychometric examination.

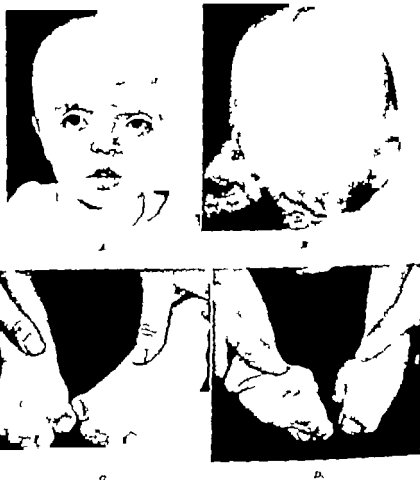


FIG. 1 (Case 8).—A, B, C, and D, Patient, 10, premature fusion of coronal suture, and syndactyly of hands and feet. The characteristic deformity of the head and the healed position of recent bilateral coronal craniotomies are evident. Lateral roundness of skull shows deformity of head ten days after operation.

In spite of the striking deformity in this group, only one patient reached the hospital for operation at the age of 6 months and only three under 1 year. None of these patients showed evidence of increased intracranial pressure.

The incidence of associated congenital anomalies in these cases has been high. In the first case, persistent enlarged parietal foramina of the skull; in the second, large parietal bone defects and buccal ulcers; and in four others

syndactylism of all four extremities (Fig. 7). If strabismus, ptosis, and exophthalmos were present before operation, they seemed to improve slowly months or years after operation (Figs. 8 and 9).



FIG. 8 (Case 3).—A, B, C, and D. Pre- and postoperative photographs of patient with premature closure of coronal sutures. The age of 4½ yrs. he has normal intelligence and appearance has improved in the 3 yrs. his "passed" younger brother of the girl has had craniotomy of coronal suture.

Surgical treatment: these cases has consisted of coronal craniectomy either in one or two stages, removing a 10 cm strip of bone extending from one squamosal suture cross the midline to the other. In three cases, bilateral subtemporal decompressions were also performed. One patient had coronal craniectomy repeated two years after the original operation, which was performed at the age of 6 months.

Most of the children in this group have been operated upon at a relatively late age and in none of them has there been a striking change in the shape of the head within a few weeks of operation. The one child in this series who has been followed to the age of  $9\frac{1}{2}$  years has shown improvement in the contour of the head and has developed normally. Earlier operation, that is, in the first two or three months of life, should do much to improve the gross cranial deformity evident in all of these children.



A



B

Fig. 3 (Case 8).—A and B. Anteroposterior and lateral roentgenograms of skull show the transverse diameter typical of premature closure of the coronal suture. The forehead high and the head brachycephalic.

#### *Premature Closure of Two or More Sutures—*

*Premature closure of sagittal and coronal sutures.* Four children were seen in whom there was premature closure of the sagittal and coronal sutures, the other cranial sutures being patent. One of these showed an additional deformity characteristic of fusion of the metopic suture, a very pointed forehead. Operation was carried out at the age of 3 months and when last seen, at the age of 8 months, there was improvement in head shape as well as apparently normal mental development. In contrast to the first patient a second child came to the hospital for operation at the age of  $5\frac{1}{2}$  years. The sequence of closure of her cranial sutures is not known but the forehead was broad and high. There was also asymmetry of the head, presumably due to closure of one side of the coronal suture before the other. The deformity in both of these children was that of a brachycephalic head with increase in height of the forehead. The third patient was seen only once in the hospital because of peculiar deformity of the head at the age of 12 years. Roentgenograms

showed closure of the coronal and sagittal sutures and admission to the hospital was advised but refused. The roentgenograms in this instance also showed a very high forehead and a brachycephalic skull with accentuation of digital markings. At the age of 23 this patient was reported to be in the United States Navy. Only one patient in this group exhibited any other anomaly. That child had bilateral syndactylism of hands and feet.

Two of these patients have had primary operations too recently to determine final results and a third had no operation. The fourth patient showed no retardation before operation at the age of  $4\frac{1}{2}$  years and has continued to develop normally. The youngest child showed papilledema bilaterally before operation and this was relieved by operation. None of these children has shown distinct evidence of retardation and it can only be surmised that this combination of suture closure is a serious one but does not carry with it as ominous a prognosis as other combinations to be discussed here.

*Premature closure of sagittal and lambdoid sutures.* In the experience of The Children's Hospital, there have been three patients with premature closure of the sagittal and lambdoid sutures. Each of these showed evidence of obvious mental retardation when first seen in the hospital. One of these first operated upon at the age of 23 months, has improved and is considered by her family to be bright but objects a psychometric examination showed significant retardation. The other two patients, first treated surgically at the age of approximately 3 years, have shown no real improvement and were retarded mentally when last seen. This group of cases showed frequent association of other congenital anomalies. One child had multiple congenital anomalies of the vertebrae another had exophthalmos and strabismus, which were not secondary to increased intracranial pressure.

Surgical treatment in each of these children included linear craniectomies and subtemporal decompressions, none of the procedures being done earlier than the age of 23 months. Pneumoencephalograms in two of these patients showed gross ventricular dilatation and cortical atrophy.

It is of some interest that in two of the three patients of this group the coronal suture was distinctly open at the age of approximately 3 years. At the age of 4 in one case and in the other there was roentgenographic evidence of closure of all of the cranial sutures. The third patient showed some progression toward complete closure of all sutures at the age of 5 years. It is obvious, therefore, that these three patients if seen for the first time at more advanced ages, would have been included in the oxycephalic group with complete closure of all cranial sutures.

*Premature closure of All Cranial Sutures.*—Patients with premature closure of all the cranial sutures present a reasonably consistent deformity of the head but the contour may vary slightly depending on the sequence in which the sutures fuse. The head is usually small pointed at the vertex, with the eyes prominent. One is divided such cases into true oxycephaly and telecephaly.

oxycephaly. In the first group the closure of sutures is present at birth. In the latter it develops sometime in the postnatal period or in later infancy or childhood.

According to previous reports in the literature these children have commonly shown not only mental deficiency but blindness as well. Many explanations of the blindness associated with synostosis of all the sutures have been suggested, the most reasonable being that optic atrophy results from chronically increased intracranial pressure. Most writers have agreed that if blindness does not develop before the age of 8 years, it rarely appears.

This series includes six patients with clinical and roentgenologic evidence of closure of all the cranial sutures. One of these patients was operated upon first at the age of  $3\frac{1}{2}$  months, one at 4 years, eleven months, one at 5 years, one at 6 years, and one at  $7\frac{1}{2}$  years. Only one of these patients showed any associated congenital anomaly. That child first had a roentgenogram taken at the age of  $7\frac{1}{2}$  years and showed fusion of all sutures. Her head contour is typical of those cases with closure of the coronal suture. She had syndactylism of hands and feet.

On admission to the hospital, the two youngest patient showed definite papilledema bilaterally. Both of these showed complete resolution of the papilledema after decompressive operation. The other three patients, all seen after they were 5 years of age, had various degrees of optic atrophy but no demonstrable loss of visual acuity. None of these has shown any progression of visual disturbance and it seems fair to assume that surgical procedures were effective in preventing any further loss of vision. All of this group showed accentuation of digital markings in the skull by roentgenographic examination (Fig. 10).

The type of surgical treatment carried out has varied as experience has increased. In three of the earlier patients, subtemporal decompressions combined with linear craniectomies were done. In the last two, linear craniectomies were performed without subtemporal decompressions. The three older patients of this group were obviously retarded mentally on admission to the hospital. One of them showed no significant improvement after operation, the other two were considered improved postoperatively by their families, but were nevertheless retarded. One is slightly retarded with an I. Q. of 99.

The fourth patient first showed closure of the coronal and sagittal sutures at the age of about 18 months, but at that time there was no evidence of increased intracranial pressure, no mental retardation, and no visual disturbance. During the fourth year his mental development became noticeably retarded and there was bilateral papilledema. Subtemporal decompressions were performed. Subsequently coronal craniectomy was also done and the latter operation was repeated three years later. The patient has recently been seen at the age of 11 years and, although small for his age, he is not mentally retarded and has adequate if not completely normal vision (Fig. 11).

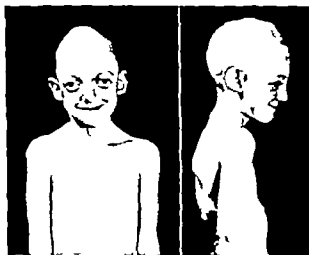
A report of the youngest patient in this group is presented in some detail (Fig. 12).

**CASE REPORT.**—R. C. male infant, was  $3\frac{1}{4}$  months old when first admitted to the hospital. Birth weight was 4 pounds, 12 ounces. Closure of the sutures had been noted at birth and confirmed by roentgenogram at 5 days of age. After birth the infant gained weight slowly and had repeated cyanotic attacks, particularly after feedings. The patient was beginning to hold up his head and to recognize objects, at the age of  $3\frac{1}{4}$  months.

Family history was noncontributory.

Physical examination revealed temperature  $98.5^{\circ}$  F, pulse 120, respirations, 30, blood pressure 100/65.

The head measured 24.5 cm. forehead to vertex narrow. The head tapered toward the midline in the posterior parietal region. The veins of the scalp were dilated and the hair



A

B



C



D

FIG. 1 (CASE 1).—C and D. Premature closure of cranial sutures. Frontal view shows small head, absence of sutures, recession of digital impressions, and widening of accessory sulci.

was very red. The fontanelles were closed. The eyes were prominent but there was no definite exophthalmos. The optic discs showed papilledema of 1 to 2 diopters. There was noisy breathing through the nose and mouth but no organic obstruction was found. There was a systolic murmur over the precordium and questionably enlarged heart. The remainder of the examination was normal.

During the patient's course in the hospital there was choking, respiratory obstruction, and transitory cyanosis on repeated occasions during feedings.



A

B



C

D

— at onset of

Operations were performed at the age of 1½ months. On two occasions A strin, 100 mg. per kilogram was administered per rectum but on each occasion the child became cyanotic, showed Cheyne Stokes respirations and apnea, and required artificial respiration. Drop ether had the same general effect. On a third occasion bromide was administered by stomach tube and corneal reflexes were carried out under local procaine anesthesia. In similar manner lambdoid craniectomy was done eleven days later. Polyethylene film was inserted over the bone edges of the craniectomies.



FIG. 12 (Case 41).—A, B, and D, Pre- and postoperative photographs of an infant with premature closure of 11 cranial sutures. (Preoperative) Acetabular constriction, papilloedema, cranial nerve palsies, and acute exophthalmos relieved by coronal and lambdoid craniectomies.

Postoperatively the patient did extraordinarily well. There were no further cyanotic attacks and the noisy respiratory sounds became less marked and finally disappeared. The head showed rapid enlargement. In proving if the residual sutures particularly if the coronal. Physical and mental development progressed normally the papilloedema disappeared, and vision was grossly normal.



was very red. The fontanelles were closed. The eyes were prominent but there was no definite exophthalmos. The optic discs showed papilloedema of 1 to 2 diopters. There was noisy breathing through the nose and mouth but no organic obstruction was found. There was a systolic murmur over the precordium and a questionably enlarged heart. The remainder of the examination was normal.

During the patient's course in the hospital there was choking, respiratory obstruction, and fits every 3 or 4 hours on repeated occasions during feedings.



A

B



C

D

Case 1—A B C and D A patient with irreversible closure of coronal and sphenoidal sutures. (Anteroposterior radiograph taken after birth effort—1 1/2 times less normal)

Operations were performed at the age of 2½ months. On two occasions Avertin, 100 mg per kilogram, was administered per rectum but on each occasion the child became cyanotic showed Cheyne Stokes respirations and poors, and required artificial respiration. Drop ether had the same general effect. On third occasion brandy was administered by stomach tube and coronal craniectomy was carried out under local procaine anesthesia. In similar manner lambdoid craniectomy was done eleven days later. Polyethylene film was inserted over the bone edges of the craniectomies.

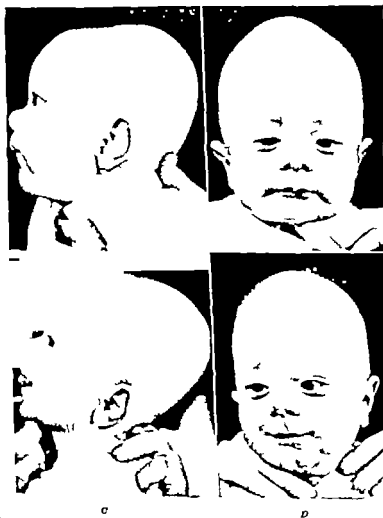


FIG. 12 (Case 3).—A, B, C and D Pre- and postoperative photographs of an infant with premature closure of all cranial sutures. Proper thymic aspiration, papilledema, cyanotic attacks, and mild exophthalmos relieved by coronal and lambdoid craniectomies.

Postoperatively the patient did extraordinarily well. There were no further cyanotic attacks and the noisy respiratory sounds became less marked and finally disappeared. The head showed rapid enlargement with spreading of the artificial sutures particularly of the coronal. Physical and mental development progressed normally the papilledema disappeared, and vision was grossly normal.

At the age of 8 months the child developed severe respiratory infection and died of overwhelming pneumonia twenty-four hours later. Post mortem examination showed pneumonia to be the cause of death. The bronchial tree and the cardiovascular system are free of congenital anomalies. The head showed the coronal craniectomy to be 4 to 5 cm. in width compared to its original width of 1 cm. There was no increased intra-cranial pressure. There was mild degree of platybasia. It was of particular interest that the brain weighed slightly more than normal for the age of the patient and serial coronal sections showed no abnormalities.

There was no evident foreign body reaction to the polyethylene film over the bone edges of the craniectomy. New bone had reformed from the periosteum and had attempted to grow over the layer of film to close the defect in the skull.

*Other Types of Synostosis Crani*—Occasionally patients are seen in whom one side of the coronal suture only has closed leaving all of the other sutures patent. This results in an asymmetry of the head which has been termed plagiocephaly (Fig. 13). In the experience of this clinic, such mild deformities have not interfered with the normal growth of the brain and it has not been



Fig. 13 (Case 26).—Premature closure of one coronal suture in an infant giving an asymmetrical forehead. This patient later developed premature closure of both sides of the coronal suture and of the sagittal suture, requiring operation.

necessary so far to treat such patients urgently. It is of extreme importance however to follow these patients closely with periodic physical and roentgenographic examinations because closure of one-half of the coronal suture may be the precursor of closure of the other half or of closure of the sagittal suture, a sequence of events which probably occurred in one of the patients discussed previously.

More frequently than plagiocephaly one sees normal children with markedly pointed foreheads. This deformity called trigonocephaly is the result of premature closure of the metopic suture. Usually this suture is obliterated at the time of birth although it may persist for months or years. In order to cause deformity of this type, closure of the metopic suture must occur in utero (Fig. 14).

This deformity has been found to be of no clinical significance so long as the other suture lines are normal and it has been felt that no surgical treatment is necessary except when the deformity is so marked as to warrant surgery for the cosmetic effect.

#### SURGICAL TREATMENT

It has been the experience of most neurosurgeons that any decompressive operation performed in infants for *synostosis cranii* is effective for a relatively short time because of the tendency of the bone to heal rapidly. Reports by King,<sup>12</sup> Woodhall, Faber and Towne and others have indicated that to gross palpation and to roentgen ray visualization operative skull defects often show firm healing in four months. Judging from the experience at The Children's Hospital, it is doubtful if simple linear craniectomies performed in infants permit expansion of the skull longer than four to eight months. Cases have been observed in which 1 cm. strips of bone have been removed from each paravagittal region; roentgenograms taken twelve months later showed complete healing with almost no evidence of the previous craniectomies. Others have shown solid bone bridges across the craniectomies within six months, thus preventing further skull expansion.



Fig. 1 — (a) and (b) Characteristic deformity of forehead in closure of the multiple sutures. This deformity ordinarily requires no surgical treatment.

Many types of operations for the relief of craniosynostosis have been described since Lannelongue in France in 1890 and Lane<sup>13</sup> in the United States in 1897 first used linear craniectomies for the relief of craniosynostosis. Subtemporal decompression have been used widely during the past forty years and apparently with some success. Numerous other techniques have had their proponents, but there is a growing feeling that linear craniectomy in the region of the fused sutures is the most physiologic method for allowing a crowded or deformed brain to grow in normal fashion.

While any one of several types of craniectomy produces satisfactory immediate relief of cerebral compression in older children all of the methods previously reported have been inadequate for treatment of premature craniosynostosis in early infancy. The rapid rate of bone regeneration in this age group has resulted in reclosure of artificially created sutures or decompressions before the period of rapid brain growth has been completed. This has necessitated secondary operations frequently in the series of cases treated at The Children's Hospital. Of fourteen patients under 2 years of age treated by linear craniectomy and followed for more than one year eight have required secondary procedures because of bony fusion of the craniectomies.

Experimental studies were therefore instituted in the laboratory to discover methods suitable for use in infants to prevent or retard significantly the healing of artificial suture lines. These experiments have been reported by Ingraham, Matson and Alexander.<sup>24</sup> It was found that certain inert foreign materials, including tantalum methyl methacrylate (Lucite) and polyethylene will significantly retard the healing of artificial cranial sutures in young animals. Of these three materials, polyethylene in the form of a thin film is the easiest to handle technically and is least expensive; it has therefore been adopted routinely for use over the cut edge of artificially created cranial sutures in patient. Since this experimental work was completed, Simmons and Perton have reported the use of tantalum foil over one margin of artificially created sutures in two infants with craniosynostosis.

*Present Technique*—For premature closure of the coronal suture a coronal craniectomy is performed, extending from one parietal suture across the vertex to the other. Lambdoid craniectomy is similar done for premature closure of that suture. Frontal suture closure paranasal craniectomies are performed leaving a strip of bone 3 cm in width in the midline over the sagittal sinus. These craniectomies should also extend beyond the lambdoid and coronal sutures. The operations are performed under ether anesthesia.

Although new bone forms from the dura which is the endosteum the periosteum reforms bone much more rapidly. The only significant bridges across skull defects in the laboratory animal were seen on the external surface, having regenerated from periosteum. This has led to a wide removal of periosteum adjacent to craniectomies in patient. After opening the scalp therefore the periosteum is resected for a distance of at least 3 cm on each side of the proposed craniectomy.

A linear craniectomy is performed by making multiple burr holes 5 to 6 cm apart either to the sutures of the coronal suture or adjacent to it. These burr holes are connected by a Gigli saw removing strips of bone 10 to 15 cm in width. The burr holes may be connected by saws in infants under 4 to 6 months of age. The dura is not opened but it is separated from the bone about 15 cm to either side of the linear craniectomy. Drill punch holes 2 mm in diameter are made 6 mm back from each bone edge at intervals of 5 cm.

**Fig. 17**



Fig. 17.—Polyethylene film folded over curved malleable retractor prior to sterilization by beta rays. It retains the curved contour which facilitates the insertion of the film over the bone edges. At the top, the film has been removed from the metal retractor.

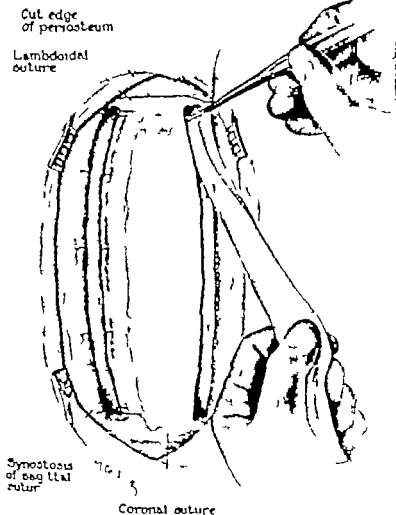


Fig. 18.—Operative field in case of premature closure of the sagittal suture. Parasagittal craniotomy has been done; the periosteum widely resected. Polyethylene film has been inserted on one side and is being fixed in position on the other side.

Polyethylene film 0.005 cm. thick is cut in strips 2.5 cm. wide and about 25 cm. long. It is folded over the edge of a malleable abdominal retractor bent according to the contour of the infant's head. The folded film is held in position with tape or large caliber string pulled firmly but not tightly (Fig. 15). The malleable retractor and the film are wrapped in a gauze sponge and boiled in water for thirty minutes. Autoclaving will change the plastic film into an amorphous mass, but boiling alters the film only in making it maintain the U-shape it assumed during the boiling process.

A piece of the sterile U-shaped polyethylene film is then trimmed so that each limb is about 1.0 cm. wide and the length conforms exactly to the length of the craniectomy. It is inserted over the margins of the craniectomy and held in place by silk sutures passed through the drill holes and the film (Fig. 16). The film tears only with strong force. It can be handled easily, therefore, and with a little experience made to lie smoothly over inner and outer bone surfaces. The film is placed over both edges of each craniectomy. The scalp wound is then closed in layers with interrupted sutures of fine silk.



A

B

Fig. 17 (Case 37).—A and B. Anteroposterior and lateral roentgenograms to be taken after bilateral parietal craniectomy in an infant. Characteristic deformity of brow very clearly of the sagittal suture is evident. Craniectomies carried through coronal and lambdoid sutures.

Twenty-two linear craniectomies using polyethylene film have been performed on nineteen patients in the past twelve months. There have been no postoperative deaths, no wound infections, and no serious complications other than a severe laryngitis and tracheitis in one patient. The longest follow-up period for any patient is twelve months. Pericranium was not resected widely in that patient and film was placed only over one bone edge. There has been bony healing from the bone edge not covered with film but the craniectomies are still palpable. The patency of these craniectomies performed with wide removal of pericranium and wrapping of both bone edges

\*Obtained from Harvard Plastic Company 1108 Boylston St., Boston, Mass. Now available also in thinner sheets of 0.0025 cm.

with film has been much more satisfactory. The length of time since operation of most of the cases is insufficient to justify any final conclusions regarding the effectiveness of the polyethylene film in maintaining the patency of artificially created cranial sutures but the early results are most promising (Fig. 1.)

#### SUMMARY AND CONCLUSIONS

1 Because of the rapid growth of the brain during the first year of life it is to be expected that the best results from surgical treatment of premature closure of the cranial sutures will be obtained during this period. This has been confirmed in the series of cases described in this report. This fact places the responsibility for early suspicion and diagnosis of this condition upon the obstetrician and the pediatrician.

2 Of the fifty cases presented here from The Children's Hospital forty four patients have been treated by surgical procedures. (See Chart I and Tables I and II.) Twenty or 40 per cent were retarded to some extent before operation. 50 per cent of those treated surgically showed retardation after operation. Divided into separate groups, 94.4 per cent of the sagittal group 37 per cent of the coronal group and 83 per cent of those patients with two or more sutures fused showed mental retardation.






Sagittal (29)	
Coronal ( )	
Sagittal and Coronal ( )	
Sagittal and Lambdoid (2)	
All Cranial sutures (8)	

Chart I—Craniosynostosis sutures involved

3 In the entire series, twenty patients received primary surgical treatment before the age of 1 year. Of this group there was only one definitely retarded patient.

4 Many patients, particularly those treated before 1940 came to the hospital at ages ranging from 3 to 7 years. They were usually retarded when brought in for medical aid and little was to be expected from any surgical procedure. In spite of this and often to the surprise of the physician there was marked improvement in the patient's behavior at home.

5 Premature closure of the sagittal suture was the most common single type of synostosis found. It was involved in all the patients of the entire series except eight with premature closure of the coronal suture alone. Congenital anomalies are more frequently found in association with closure of the sagittal suture than in the normal population. No single anomaly has been found to predominate.

6 Premature closure of the coronal suture is usually associated with other congenital anomalies, particularly syndactylism of hands and feet.



TABLE I. AGE WHEN DEFORMITY WAS FIRST NOTED

AGE	NUMBER OF
	TEENY
At birth	33
1-2 months	6
3-6 months	2
6-9 months	4
9-12 months	1
Over 12 months	2
Unknown	3
Total	50

TABLE II. RELATION OF RESULTS TO INTERVAL BETWEEN ONSET AND OPERATION

	TOTAL	RETARDED
Less than 1 year	22	3
1-2 years	10	4
2-4 years	4	3
4-6 years	4	3
Over 6 years	4	3
Unoperated	6	4
Total	50	20

7 Patients observed over several years have been found to show gradual closure of other cranial sutures than those originally involved. It is, therefore, imperative to follow these patients with periodic physical examinations, mental evaluation, and roentgenograms.

8. The forty-four patients treated surgically have had a variety of decompressive operations, all of which have apparently been effective to some degree. Linear craniectomy with polyethylene film inserted over the bone edges to retard regeneration of bone has been adopted as the operation of choice. The present technique for this procedure has been described in detail.

9. In general the prognosis for mental development of a patient with premature closure of the cranial sutures treated under the age of 1 year is excellent but if synostosis is evident at birth, surgical therapy should not be delayed more than a few weeks. It is inadvisable to delay operation until mental retardation becomes evident.

10. The mortality for operation on infants with craniosynostosis is negligible when proper supportive measures are provided.

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# THE ANTIBACTERIAL EFFECTS OF G-6, G-11,<sup>†</sup> AND A-151,<sup>‡</sup> WITH SPECIAL REFERENCE TO THEIR USE IN THE PRODUCTION OF A GERMICIDAL SOAP

PHILIP B. PRICE, M.D. AND ALBERTA BONNETT  
SALT LAKE CITY, UTAH

(From the Department of Surgery, University of Utah School of Medicine)

EVER since the time of Robert Koch (1881) unsuccessful attempts have been made to produce a germicidal soap. The need for such a soap is obvious. The skin acts both as a barrier to microbe invasion of the body and as a carrier of potentially dangerous germs. Use of an effectively bactericidal soap would from both standpoints reduce the chances of infection.

Mechanical cleansing of skin with ordinary nonmedicated soap removes dirt, oils, and fats, as well as many loosely attached contaminating microorganisms, but the resident bacterial flora is not easily reduced.<sup>1</sup> Streptococci, pneumococci, diphtheria and influenza bacilli, and other susceptible pathogenic microorganisms are sometimes observed to have disappeared from hands after washing with ordinary soap, but staphylococci, colon bacilli, and sporulating anaerobes are more resistant. Yellow kitchen soap is more germicidal than bland white toilet soaps, as Kelly<sup>2</sup> demonstrated long ago, but that advantage is offset by its harsh irritating effect on skin. Pohle and Stuart<sup>3</sup> in 1941 reported that rosin soaps, or coconut oil soaps containing rosin, are more effective than ordinary soaps in degreasing the skin.

Such studies are complicated by the tendency of many extraneous bacteria to disappear spontaneously from the cutaneous surface. This self-disinfecting power of skin remains poorly understood despite researches of Schlemm, Arnold and associates, Norton and Novy, Burtenshaw and others.

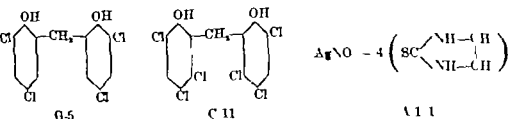
It might appear easy at first thought to produce a germicidal soap simply by incorporating a germicide in soap. Many such preparations have been made and some of them have been marketed with extravagant and unwarranted claims.

According to Gump a germicide added to soap should fulfill the following conditions. It should retain its germ-killing powers in soap. It should not react with the soap constituents, or with the moisture contained in the soap. It also should not be influenced by the free alkali of the soap, nor by the alkalinity produced by the hydrolysis of the soap in the water. It should not be volatile and should not have a disagreeable odor. It should be relatively nontoxic and should not be irritating to the skin, be a sensitizer. It should not stain the skin or cause spots on the laundry.

Very few chemicals meet these requirements. In fact, none of the familiar time-honored germicidal soaps, tested by rigid standards, is found to have much disinfectant power.

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Recently a number of hitherto untried chemical compounds were found to retain a large part of their bactericidal strength in the presence of excessive amounts of soap. Some of these compounds are di-phenols, derivatives of di-phenyl, diphenylsulfide and diphenylmethane. Two of them, whose structures are indicated here have for convenience been designated G-5 and G-11. Another promising substance, a complex salt of ethylene thionurea and silver nitrate is called A-151.



G-5 and G-11 are white powdery compounds virtually insoluble in water but soluble in alcohol, acetone and dilute alkali. A-151 a colorless crystalline compound, is soluble in hot water as well, but only sparingly in cold water. These three substances have been used in a new effort to produce a truly germicidal soap.

Of the three products, the one which has received most attention is G-11. Traub, Newhall, and Fuller<sup>2</sup> reported that 4 per cent G-11 soap used regularly for a week or more causes a pronounced reduction in the cutaneous bacterial flora. They claim that a person using this soap regularly each time the hands are washed has a lower resident count after 5 minutes of washing than one who washes for 10 minutes with ordinary toilet soap. These conclusions were corroborated in general by U. Link<sup>3</sup> who employed simplified bacteriological tests, but extended his observations over a period of many months. More recently Heister<sup>4</sup> has reported similar results. We are informed that G-11 soap is now being given a clinical trial in certain selected surgical clinics.

The present investigation was undertaken as part of a large collaborative study of skin disinfectant and skin disinfection.

#### PECULIAR ASPECTS OF THE PROBLEM

The insolubility of G-5, G-11 and A-151 in water makes it necessary to employ solvents—alcohol, acetone, or sodium hydroxide—which in themselves have antiseptic action. At the same time the bactericidal or bacteriostatic effect of the solvent in dilution with water results also in precipitation of indeterminate amounts of the chemical agent to be tested. For example, a 1:100 solution of A-151 in hot water is clear, diluted with 50 parts of cold distilled water it turns cloudy, centrifuged rapidly for 1 hour a clear supernatant fluid is obtained which retains a considerable amount of bacteriostatic activity.

<sup>2</sup>In the laboratories of the Glaxo Laboratories Company.

# THE ANTIBACTERIAL EFFECTS OF G-5, G-11, AND A-151, WITH SPECIAL REFERENCE TO THEIR USE IN THE PRODUCTION OF A GERMICIDAL SOAP

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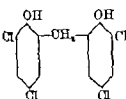
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Received for publication, Feb. 1, 1945.

\*G-5, Na-(2,4-dichloro-5-hydroxyphenyl) methanesulfonate.

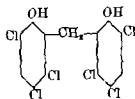
\*G-11, Na-(2,4,6-trichloro-3-hydroxyphenyl) methanesulfonate.

A-151, L. complex salt of ethylene thiosulfonate and silver nitrate.

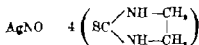
Recently a number of hitherto unused chemical compounds were found to retain a large part of their bactericidal strength in the presence of excessive amounts of soap. Some of these compounds are diphenols, derivatives of diphenyl, diphenylsulfide and diphenylmethane. Two of them, whose structures are indicated here, have for convenience been designated G-5 and G-11. Another promising substance, a complex salt of ethylene thiourea and silver nitrate is called A 151.



G-5



G-11



A 151

G-5 and G-11 are white powdery compounds, virtually insoluble in water but soluble in alcohol, acetone, and dilute alkali. A 151, a colorless crystalline compound, is soluble in hot water as well, but only sparingly in cold water. These three substances have been used in a new effort to produce a truly germicidal soap.

Of the three products, the one which has received most attention is G-11. Traub, Newhall, and Fuller<sup>2</sup> reported that 2 per cent G-11 soap used regularly for a week or more causes a pronounced reduction in the cutaneous bacterial flora. They claim that a person using this soap regularly each time the hands are washed has a lower resident count after minutes of washing than one who washes for 30 minutes with ordinary toilet soap. These conclusions were corroborated in general by Udinsky, who employed simplified bacteriological tests, but extended his observations over a period of many months. More recently Reardon<sup>3</sup> has reported similar results. We are informed that G-11 soap is now being given a clinical trial in certain selected surgical clinics.

The present investigation was undertaken as part of a large scale critical study of skin disinfectants and skin disinfection.

#### PECULIAR ASPECTS OF THE PROBLEM

The insolubility of G-5, G-11, and A 151 in water makes it necessary to employ solvents—alcohol, acetone, or sodium hydroxide—which in themselves have antibacterial action. Attempts to eliminate the bactericidal or bacteriostatic effect of the solvent by dilution with water results also in precipitation of undeterminable amounts of the chemical agent to be tested. For example, a 1:100 solution of A 151 in hot water is clear, diluted with 50 parts of cold distilled water it turns cloudy, centrifuged rapidly for 1 hour a clear supernatant fluid is obtained which retains a considerable amount of bacteriostatic activity.

<sup>2</sup>In the labor series of the Otis-Wells-Dalewarren Company.

It is believed by the manufacturers that the alkali of the soap in which G-5, G 11 and A 161 are incorporated serves to keep the chemicals in effective solution, but to what degree that is true in the presence of large amounts of water especially hard water or in culture media used for making bacterial counts, is unknown. That may be a consideration of some importance since G-5 and G-11 inhibit bacterial growth when they are present even in minute amounts.

Another difficulty arises from lack of specific antidotes or neutralizing agents for phenolic compounds. It is conceivable that, as in the case of mercurial disinfectants, G-5, G 11 and A 161 unite in some way with bacterial cells, and that this union is not broken by subsequent dilution or washing with water. The chemical still attached to or combined with, the cells may then inhibit their growth in cultures without killing them. A very common pitfall in all studies of disinfection lies in mistaking bacteriostatic for bactericidal effect. Unless a specific antidote is employed, which effectively removes or neutralizes the disinfectant being tested, gross misconceptions of its germicidal value may be obtained.

Seaton<sup>11</sup> has suggested the use of serum in media as an antidote for G-5 and G 11. Although serum probably does not neutralize these agents chemically it does liberate some of the bacteria, as shown by significantly higher bacterial counts in serum agar plates. A 161 on the other hand, can be neutralized chemically without difficulty.

Another interesting complexity of these tests is that very minute quantities of G-5 and G 11 in cultures, amounts too small to have any bacteriostatic effect, seem to result in significantly higher counts than controls show. Whether that is due to breakup of coecal clumps, or to stimulation of certain bacteria which otherwise would not grow out, or to some other effect, we do not know.

#### IN VITRO TESTS

Scores of tests were made using the three chemical agents in various concentrations against *Staphylococcus aureus*, *Staphylococcus albus* and *Escherichia coli*. A number of strains of *Staph. aureus* were utilized, one from a stock culture in our Bacteriological Laboratory, one (Strain 309) obtained from the U. S. Food and Drug Administration Division of Bacteriology, Washington, D. C., and several isolated from the resident flora of our own hands. Results with these different strains were similar. Most of our tests consisted of culturing known numbers of vigorously growing test bacteria in poured agar plates. In germicidal tests, suspended organisms were exposed to graded concentrations of the disinfectant for measured lengths of time immediately before dilution and plating. In some of the tests for bacteriostasis, the chemicals were added to the bacterial suspensions before plating; in others, the chemicals were added to the agar before inoculation with test organisms. Accurate plate counts were made after forty-eight hours in incubation in order to determine as nearly as possible the precise degree of killing or inhibition produced. The following is a highly summarized report of this work.

G-5 has powerful bacteriostatic action. A concentration of 1-4,000,000 in nutrient agar culture media causes complete or nearly complete inhibition of

TABLE I. BACTERIOSTATIC AND BACTERICIDAL EFFECTS OF G-5 AGAINST TEST BACTERIA IN VITRO

TEST	ORGANISM	DILUTION OF G-5	EFFECT
G-5 in agar media	<i>Staph aureus</i>	1:4,000,000	Full inhibition
	<i>Staph aureus</i>	1:10,000,000	No inhibition
	<i>Esch coli</i>	1:50,000	Full inhibition
	<i>Esch coli</i>	1:100,000	No inhibition
G-5 in soap in agar	Mixed skin flora	1:150,000	Marked inhibition
	Mixed skin flora	1:150,000	Marked inhibition
G-5 in blood agar	<i>Staph aureus</i>		
	<i>Staph aureus</i>		
Bacteria in suspension, exposed to G-5, then cultured	<i>Staph aureus</i>		
	<i>Staph aureus</i>		

NOTE: ALLIED RE CT OR SECONDS EXPOSURE

*Staph aureus* (Table I) Less than 1:10,000,000 has little or no bacteriostatic effect. That is true whether the original solvent is acetone or sodium hydroxide. Mixed skin organisms, mostly *Staph aureus*, appear to be slightly less susceptible to the bacteriostatic effect of G-5. *Esch coli* is definitely more resistant.

The presence of blood or serum in media greatly reduces the bacteriostatic effect of G-5. A concentration of 1:1000 G-5 is required for complete inhibition of *Staph aureus* and there is no inhibition in strengths of 1:10,000 or less (Seastone noted similar effects with serum in his study of G-11).

A solution of 1:1000 G-5 in weak acetone or sodium hydroxide solution appears to be capable of killing *Staph aureus* suspended in water within 30 seconds at room temperature (about 25°C). We have not been able to convince ourselves, however, that this is all bactericidal effect and that bacteriostasis has no role in the production of negative cultures. Concentrations of G-5 1:100,000 or weaker appear to have no bactericidal effect on suspensions of *Staph aureus* in 60 seconds at room temperature.

In dilutions as high as 1:5,000,000 or even 1:5,000,000 in agar media, G-11 causes complete or nearly complete inhibition of *Staph aureus* (Table II). This bacteriostatic effect disappears when the dilutions are in the neighborhood of 1:20,000,000. *Esch coli* grows with only slight reduction of counts in 1:1,000 G-11 media. These results parallel those of Seastone who in his qualitative tests used much heavier inocula than we have employed in our quantitative experiments.

1:1,000,000 G-11 in 0.1% NaOH appears to kill suspensions of *Staph aureus* after thirty minutes exposure at room temperature but with exposures of only ten minutes normal counts are obtained (Udinsky<sup>10</sup> reported that 1:1000

TABLE II. BACTERIOSTATIC AND BACTERICIDAL EFFECTS OF G-11 AGAINST TEST BACTERIA IN VITRO

TEST	ORGANISM	CT
G-11 in agar media	<i>Staph aureus</i>	
	<i>Staph aureus</i>	
	<i>Esch coli</i>	
Bacteria in suspension, exposed to G-11 then cultured	<i>Staph aureus</i>	30 minutes
	<i>Staph aureus</i>	few killed after 10 minutes exposure



TABLE III. BACTERIOSTATIC AND BACTERICIDAL EFFECTS OF A 151 AGAINST TEST BACTERIA IN VITRO

those cultured	<i>Staph aureus</i>	1 600,000	None killed after 60 seconds exposure
	<i>E. coli</i>	1 10,000	None killed after 30 seconds exposure

G 11 will kill *Staphylococcus aureus* in five minutes at 37° C. when tested in accordance with the standard F. D. A. germicidal procedure.)

In contradistinction to G-5 and G 11 A 151 appears to be as effective against *E. coli* as against *Staph aureus*. A 151 is bactericidal for *Staph. aureus* in concentrations of 1:10,000 or stronger with one minute exposure at room temperature, but 1:500,000 has no killing action (Table III). A quantity of per cent A 151 soap sufficient to make a concentration of 1 part of the chemical in 50,000 parts of agar media causes complete inhibition of *Staph. aureus*, but a 1:100,000 concentration has no significant bacteriostatic effect. It has been noticed, however that despite the availability of thio glycolate as an effective antidote, our tests with A 151 have given less constant results than those with G-5 and G-11. The values in Table III are not to be considered exact, therefore but rather as average findings in a large number of tests.

Obviously all such in vitro tests have more academic interest than practical value. It is only when disinfectant agents are tested under conditions of actual use that their real merit can be determined.

#### SKIN DISINFECTION

These three compounds, G-5, G 11 and A 151 incorporated in soap, have been subjected to our serial basin test<sup>12</sup> which, though tedious to perform, provides more trustworthy information, we believe than can be obtained in any other way. Advantages which may be claimed for the procedure are:

1. That it differentiates between transient and resident flora of the skin, and shows specific effects of germicides upon those two groups of microorganisms.

2. That it measures quantitatively and fairly accurately the size of the original bacterial population, the effect of any given disinfectant upon that population, and the size of the population left after the disinfectant is discontinued.

3. That it enables the disturbing factor of bacteriostasis to be avoided altogether or at least to be detected and taken into account.

4. That it is designed specifically to test skin disinfectant under conditions of actual use.

That it facilitates qualitative studies of the cutaneous flora at various stages of washing or chemical disinfection

6 That it permits subsequent observations on regeneration and restoration of the cutaneous bacterial flora

The following soaps were tested:

2 per cent G-5 in small cakes of relatively hard soap

6 per cent G-5 in small cakes of similar hard soap

per cent G-11 in larger cakes of high-grade softer soap

per cent A 151 in small cakes of hard brittle soap

Since these soaps were tested uniformly under conditions of ordinary use (by scrubbing with a brush in warm water) different amounts of soap came off on the brush and skin depending on the hardness of the soap used. Comparative weights of dried cakes before and after use showed that the amounts of soap actually used each minute of scrubbing averaged

\* per cent G-5 soap, 0.473 Gm.

6 per cent G-5 soap, 0.590 Gm.

per cent G-11 soap, 1.020 Gm.

\* per cent A 151 soap 0.303 Gm.

These measurements were taken into consideration in estimating the concentration of the chemical disinfectants in lather wash water and cultures

*Bacterial Effects of Scrubbing With the Disinfectant Soaps for Single Periods of One to Ten Minutes*—In these tests the hands and arms were first scrubbed with Ivory soap in a uniform manner in a series of basins of sterile water. One of the disinfectant soaps was then substituted for the Ivory soap

TABLE IV. DISINFECTANT EFFECT OF THREE-MINUTE SCRUB WITH PER CENT G-5 SOAP  
(ORIGINAL PRICE TEST) TIME SPENT IN EACH BASIN 1 MINUTE

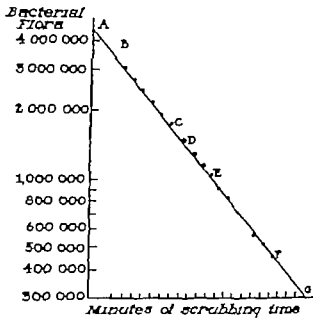
BASIN NUMBER	SOAP USED	BACTERIAL COUNT	CUMULATIVE TOTAL	ACTUAL TOTAL
1	Ivory	425,000	425,000	3,507,000
2	Ivory	440,000	865,000	3,009,000
3	Ivory	40,000	905,000	2,719,000
4	Ivory	290,000	1,195,000	2,479,000
5	Ivory	250,000	1,445,000	1,179,000
6	Ivory	173,000	1,618,000	1,903,000
7	2% G-5	19,400	1,637,400	1,750,000*
8	6% G-5	146,000	1,783,400	1,448,000
9	2% G-5	89,000	1,872,400	1,290,000
10			1,961,400	1,145,000
11			2,050,400	1,037,000
12	Ivory	129,000	2,179,400	1,057,000
13	Ivory	92,000	2,271,400	919,000
14	Ivory	49,000	2,320,400	853,000
15	Ivory	53,000	2,373,400	823,000
16	Ivory	51,000	2,424,400	777,000
17	Ivory	60,000	2,484,400	692,000
18	Ivory	92,000	2,576,400	617,000
19	Ivory	69,000	2,645,400	519,000
20			2,714,400	430,000

\*The number of bacteria left on the hands and arms after each period of scrubbing

Prepared for use by the Glaxo-Downey Company

In a second series of basins. Finally in a third set of basins scrubbing was resumed with Ivory soap. Cumulative totals of basin counts were plotted against time and the resultant curves were evaluated in relation to the washer's standard curve of bacterial population reduction by prolonged scrubbing with ordinary soap.

A typical test is shown in Table IV and Fig. 1. Concentration of G-5 in the lather in this instance was approximately 1:2000; in the washbasins (Basins 7 to 9) 1:430,000 and in the agar plate cultures, 1:4,700,000 or 1:9,000,000 depending on the size of sample plated. The lather containing G-5 was in contact with the skin for a total of about 135 seconds. All cultures of washings were made less than 5 minutes after the hands left the water. The concentration of G-5 in Basin 10 was estimated to be about 1:90,000,000 and in the subsequent washings G-5 was considered to be absent.



— least time to show straight-  
line  
reduction  
of the  
flora  
—

It is clear that in this test a three-minute scrub with per cent G-5 soap reduced the bacterial flora of the hands and arms somewhat (from 1,731,000 to 1,057,000) but that this reduction is very little more than would have been accomplished by the use of ordinary soap for a similar period of time. Obviously

TABLE 1. ED ACTS OF FREQUENT WASHING WITH PER CHA 0-11.50

SUBJECT	PER CENT WASHING (NO. OF WASHES)	NO. OF WASHES (NO. OF WASHES)	TOTAL BACTERIAL FLORA			RESIDUAL BACTERIAL FLORA		
			EXPECTED	OBSERVED	REDUCTION <sup>a</sup> (%)	EXPECTED	OBSERVED	REDUCTION <sup>a</sup> (%)
A	10 h (3x)	7	18,000,000	1,000,000	11.0	7,500,000	1,100,000	14.0
B	10 h (7x)	7	18,000,000	1,400,000	1.0	16,000,000	4,400,000	6.0
A	2 days	7	8,500,000	1,700,000	21.0	7,500,000	1,100,000	14.0
B	2 days	7	18,000,000	2,200,000	1.0	16,000,000	1,900,000	11.0
B	4 days	7	18,000,000	0,900,000	5.0	16,000,000	550,000	7.0
A	7 days	5	4,700,000	10,000	8.1	4,000,000	200,000	5.0
B	11 days	7	18,000,000	620,000	3.4	16,000,000	620,000	3.5
A	16 days	11	8,500,000	470,000	5.5	7,900,000	500,000	4.0

PER CENT OF DISCOMFORT DUE TO USE OF 1% CHA 0-11.50

SUBJECT	PER CENT WASHING (NO. OF WASHES)	NO. OF WASHES (NO. OF WASHES)	TOTAL BACTERIAL FLORA			RESIDUAL BACTERIAL FLORA		
			EXPECTED	OBSERVED	REDUCTION <sup>a</sup> (%)	EXPECTED	OBSERVED	REDUCTION <sup>a</sup> (%)
A	7 days	7	1,000,000	17,000,000	100.0	16,000,000	16,000,000	0.0
B	14 days	14	8,500,000	19,200,000	51.0	7,900,000	1,400,000	14.0

<sup>a</sup>Other ed. Data divided by expected flora

most of the bacteria removed while scrubbing with the G-5 soap were recoverable in viable form in the washings of Basins 7 to 9. Whether the 262,000 bacteria not accounted for (the absolute total after Basin 8 minus the absolute total of Basin 7) were killed by the chemical during the three-minute lather period, were inhibited in culture media, or represent technical error we do not know.

A comparison of these results with the *in vitro* findings of Table 1 is instructive.

From many such tests we have drawn the following general conclusions:

1. None of the disinfectant soaps under investigation is much superior to ordinary nonmedicated soap when used for single brief periods of washing or scrubbing.

2. Of the four preparations tested, 5 per cent G-5 soap was the most effective, and 2 per cent A 151 least effective, but only by narrow margins.

3. The G-5 soap preparations were slightly irritating to skin, however, whereas G 11 and A 151 soaps were quite innocuous.

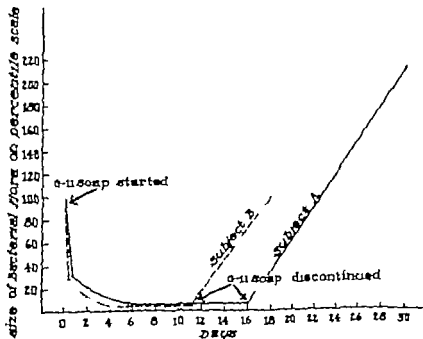


Fig. 2.—The bacteriologic effects of washing the hands repeatedly with 5 per cent G-11 soap. Restoration of the cutaneous bacterial flora after cessation of the disinfectant soap.

**Bacteriologic Effects of Repeated Frequent Washing With 5 Per Cent G 11 Soap**—Table V and Fig. 2 summarize the result of a number of tests made on subjects A and B. These two individuals prior to the tests had for various periods of time used G 11 soap every time they washed or bathed. Other disinfectant agents, such as alcohol had not been used for several days, prior to each test, as shown in Column 3. What their bacterial counts would have been

had the disinfectant soap not been used must be estimated by averaging a large number of preliminary control tests consequently the expected values listed in the table are only approximations. By the same token, the effects of frequent washing with G-11 soap expressed in terms of percentage reduction of the usual flora, are no more than approximations.

In general the tests seem to show that the bacterial flora of skin is reduced by frequent repeated washing with 2 per cent G-11 soap, maximal reduction being reached after four to seven days of use. Continued use of the soap does not reduce the bacterial population further but does keep it at a low level of about 5 per cent of the usual number.

When use of G-11 soap is discontinued, the cutaneous flora regenerates promptly and returns to normal proportions in approximately seven days. A similar regeneration rate occurs after disinfection of the skin by other means, which suggests that G-11 soap has little if any lasting effect in keeping the cutaneous flora low once its use is discontinued.

Additional tests were made with five members of our operating room staff three surgical residents and two nurses. Since these individuals did not have standard curves established the absolute effects of G-11 soap on their cutaneous microbial populations were not determined. Bacterial counts of serial basin washings indicated, however, that the usual flora of the hands and arms of these persons were markedly reduced by daily frequent washing with 2 per cent G-11 soap for one week, but that failure to use the soap constantly resulted in prompt return to higher counts. Many transient bacteria were found on all the hands, even when the disinfectant soap was being used regularly. The impression was gained that the soap was more effective in keeping the resident flora low than in preventing the skin from picking up contaminants.

It was estimated that in using 2 per cent G-11 bar soap for scrubbing the concentration of the chemical in lather was about 1/600, and that a similar concentration could be obtained by employing a liquid soap containing 0.2 per cent G-11. Accordingly this latter preparation was placed in soap dispensers in the operating room, where for six months it was used unwittingly by a large number of persons in routine preoperative scrubs. No ill effects upon the skin were noticed. On the other hand, tests made on representative individuals showed that their cutaneous bacterial flora was on the average no lower than when ordinary nonmedicated liquid soap was employed. In order to keep the bacterial flora significantly reduced, it was necessary for these individuals to keep cakes of G-11 soap in their rooms and on the wards where they could be used many times daily.

Thorough qualitative studies were not made of organisms found in washings before and after use of G-11 soap but differential counts made in representative experiments showed that the proportionate number of yellow pigment producing surface colonies was not significantly altered by the use of G-11 soap.

#### MISCELLANEOUS OBSERVATIONS

A number of patients having elective clean operations were given cakes of 2 per cent G-11 soap with instructions to bathe the site of operation several

most of the bacteria removed while scrubbing with the G-5 soap were recoverable in viable form in the washings of Basins 7 to 9. Whether the 263,000 bacteria not accounted for (the absolute total after Basin 6 minus the absolute total of Basin 7) were killed by the chemical during the three-minute lather period, were inhibited in culture media, or represent technical error we do not know.

A comparison of these results with the *in vitro* findings of Table I is instructive.

From many such tests we have drawn the following general conclusions:

1. None of the disinfectant soaps under investigation is much superior to ordinary nonmedicated soap when used for single brief periods of washing or scrubbing.

2. Of the four preparations tested, 6 per cent G-5 soap was the most effective and 1 per cent A 151 least effective, but only by narrow margins.

3. The G-5 soap preparations were slightly irritating to skin, however, whereas G 11 and A 151 soaps were quite innocuous.

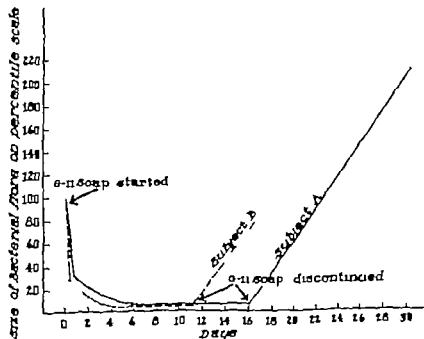


FIG. 1.—The bactericidal effects of washing the hands frequently with 6 per cent G-11 soap: restoration of the cutaneous bacterial flora after discontinuance of the disinfectant soap.

**Bacterial Effects of Frequent Washing With 6 Per Cent G 11 Soap**—Table I and Fig. 1 summarize the results of a number of tests made on subjects A and B. These two individuals prior to the tests had for various periods of time used G 11 soap every time they washed or bathed. Other disinfectant agents, such as alcohol, had not been used for several days prior to each test, as shown in Column 3. What their bacterial counts would have been

than G 11 throughout the entire institution. Under such conditions it might be expected that nurses, interns, residents, maids, orderlies, and cooks would all carry fewer bacteria on their hands than they do with ordinary soap.

A word of caution should be added, however. G 11 soap has its limitations. It would be unfortunate indeed if those who use the soap permit their enthusiasm to engender a false sense of security against infection. Since effective reduction of the resident bacterial population of skin depends so largely on the frequent and unremitting use of G 11 soap, and since a potentially dangerous transient flora may at any time be present on the hands, it would seem unwise to discard other chemical germicides and depend entirely upon G 11 soap for skin disinfection. We strongly recommend for the present at least, that the customary preoperative scrub and hand disinfection routine be carried out in full even though G 11 soap has been used. Likewise the field of operation should be treated as heretofore with germicidal solutions immediately before draping. Disinfection of the skin is difficult and uncertain at best. The present well established methods of skin disinfection may be supplemented to advantage but probably should not be supplanted, by the use of G 11 soap.

It has been suggested that traces of G 11 on skin simply inhibit proliferation of the resident flora, and that this action may protect the operative wound from a torn glove. Unfortunately there is little evidence to support such a contention. The action of G 11 on skin is clearly bactericidal as well as bacteriostatic. Surviving microorganisms which come off hands which have been washed with G 11 soap grow without inhibition in ordinary culture media (see Table IV and Fig. 1). It would not, therefore, be safe to assume that similar organisms escaping through a torn glove are unable to live and multiply in a wound.

#### SUMMARY AND CONCLUSIONS

Three new chemical compounds, for convenience designated G-5, G 11, and A 151, have been used in a fresh attempt to produce a truly germicidal soap.

Investigation of the antibacterial power of these compounds is fraught with unusual difficulties because of their insolubility in water, the bacteriostatic effects of even minute traces of the substances in culture media, and lack of effective neutralizing agents for G-5 and G 11.

In vitro tests show that all three compounds, and G 11 in particular, are powerfully bacteriostatic, but their germicidal activity is less impressive.

The three compounds incorporated in soap have been tested under conditions of actual use by means of our serial basin method. This test, in our opinion, gives more information and more reliable results than any of the simplifications of the test which have been employed by other investigators.

Single periods of scrubbing for one to ten minutes with these disinfectant soaps do not reduce the bacterial flora of the hand and arms more rapidly than similar scrubs with ordinary nonmedicated soap.

Two per cent G 11 bar soap used many times daily for four or more days reduces the resident bacterial flora of skin to about 5 per cent of its ordinary size. Continued use of the soap several times every day appears to keep the



times daily for four or more days prior to surgery. At the time of operation the skin was disinfected in the customary manner with alcohol ether and a mercurial or iodine. None of these patients showed any infection or inflammation in the wounds. Equally good results were obtained, however in a parallel group of cases in which G 11 was not used. Obviously a clinical test of this sort is without significance. The incidence of postoperative infection in any group of patients is the net result of so many variable factors, difficult or impossible to control, that it cannot be relied upon to measure the influence of any one variable—in this instance the use or nonuse of G 11 soap.

Fresh scratches and abrasions of the skin washed with G 11 soap smarted slightly and became mildly inflamed, but no more perhaps than when any other soap of equal alkalinity was employed.

One individual with acne of the face has been kept under observation for more than eighteen months during which time 2 per cent G 11 soap has been used intermittently. Although the soap has not cured the acne its repeated daily use for extended periods of time definitely reduced the incidence of pustules, and each time the soap was discontinued, the number of infections increased.

G 11 is reported by Gump to be relatively nontoxic when given orally to guinea pigs. Injected intravenously however in 0.01 N NaOH solution G-3, G 11 and A 151 were found by us to be highly toxic. As little as 35 mg. in dogs weighing 7 or 8 kilograms usually caused death within a few minutes, characterized by convulsive movements, sudden respiratory cessation, and widespread intravascular clotting of blood. The remaining fluid blood had negligible bacteriostatic power. The 0.01 N NaOH solution alone had no such effect.

#### COMMENT

Washing or scrubbing leaves on the skin a film of soap which is not entirely removed by ordinary rinsing. A thin layer of G 11 probably persists on the hands for some time after each washing and is responsible for the slow but pronounced reduction of the resident bacterial flora which occurs whenever the disinfectant soap is used many times daily for several days. If that assumption is correct any washing without G 11 soap would be disadvantageous in that the G-11 on the skin might thus be washed away permitting regeneration of the bacterial flora.

There can be little doubt that G 11 soap has real merit, and that used properly it can contribute materially to the perfection of aseptic surgical technique. Patients preparing for elective operations would do well to bathe the field of operation with the soap frequently (5 or 6 times a day) for four or more days preoperatively. Such routine would be far more effective bacteriologically and less harmful psychologically than the old fashioned evening ward prep of skin painting and larval dressings still in vogue in some quarters. Dentists, whose hands pass from one highly contaminated mouth to another would be well advised to wash with G 11 soap between each case. Physicians and surgeons would probably find it advantageous to use the soap regularly in their offices and homes. Hospitals might even consider using no other soap.

# ***Surgical Technique***

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## **TECHNIQUE OF INGUINAL NODE DISSECTION**

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### **INGUINAL NODE DISSECTIONS**

During the past few years there has been considerable interest in this clinic in the technique and indications for inguinal node dissection. It is common knowledge that such wounds frequently heal very slowly and rarely by primary intention.

#### **ANATOMY OF THE INGUINAL AREA**

Common usage of the term inguinal dissection has been interpreted as not only that area of the abdominal wall which is nearest the thigh, but also that area of the thigh which includes the femoral triangle. In our discussion the term inguinal will be interpreted as such.

**Blood Supply of Skin of Inguinal Area**—The skin over the inguinal area is supplied by the superficial external pudendal artery, the superficial circumflex iliac artery and the superficial epigastric artery. These in turn anastomose with the cutaneous branches of the inferior epigastric artery. The main branches of these arteries run in a fashion which parallels the inguinal ligament and the skin creases of the lower abdomen and upper thigh. As will be described later during the dissection of the skin flaps, these vessels and their tributaries can be seen very clearly just within the fatty layer of the superficial fascia of the skin (Camper's fascia). The direction of the vessels is parallel to the inguinal ligament.

**The Femoral Triangle**—The femoral trigone is a triangular space lying immediately distal to the inguinal ligament. This ligament forms the base of the triangle. The oblique lateral boundary is the medial margin of the sartorius muscle and the medial border of the adductor longus muscle. The roof consists of the fascia lata which completely covers the space anteriorly. The floor is made up of two inclined planes, which form a well marked median groove at their junction. The lateral inclined plane consists of the iliopsoas muscle invested by a thin layer of fascia. The adductor magnus and pectineus muscles, both of which are invested with fascia lata, form the median plane. The most important contents of the triangular space, included between the fascial roof and floor of the femoral triangle, are the femoral vessels and nerve and their branches. These structures, the termination of the great saphenous vein, the deep subinguinal lymph vessels and glands are embedded in a quantity of loose fatty tissue.

flora at that low level. If the soap is used only for preoperative scrubbing, but not between times, a persistently low flora is not maintained.

Washing with G 11 soap does not protect the skin from subsequent contamination with extraneous bacteria. Even when the disinfectant soap is being used regularly a relatively large transient flora may be found on the hands between washings and whenever use of G 11 soap is discontinued, regeneration of the cutaneous flora proceeds at the same rate as though the hands had been disinfected by other means.

G 11 soap does not appear to have a selective action against pathogenic bacteria on the skin. There is reason to believe that the numerical ratio between pathogenic and nonpathogenic microorganisms is approximately the same before and after disinfection with G 11 soap.

The antibacterial activity of G-5, G 11 and A 151 is greatly reduced in the presence of blood or serum. Injected intravenously these compounds are highly toxic. They probably should not be used in wounds.

Of the preparations tested, 2 per cent G 11 bar soap appears to offer most from a practical standpoint. Used rationally and faithfully G-11 soap is probably capable of contributing materially to the perfection of aseptic surgical technique, but in our judgment it should not be employed to the exclusion of the present routine postoperative scrub or the customary chemical disinfection of hands and fields of operation.

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The lymphatics of the rectum may be classified as the extramural and intramural groups. The intramural lymphatics consist of two freely communicating networks located within the wall, one the submucosal and the other the intermuscular network. These intercommunicate by radial lymph channels lying between the circular muscle fibers. The submucosal network is to a lesser extent continuous above with the pelvic colon, and below with the subcutaneous lymph channels of the anus and perianal skin. The intermuscular network lying between the circular and longitudinal muscle coats communicates with similar channels of the pelvic colon above and with those of the external sphincter below.

These intramuscular lymphatics in turn drain into the intermediary system which is located between the external muscular coat and the perirectal fat. This system drains into the lymphatics accompanying the superior, middle, and inferior hemorrhoidal arteries, which is the extramural lymphatic system. Thus, spread of a carcinoma of the rectum may occur superiorly, laterally or inferiorly.

The lymphatics of the anus drain mainly into the superficial nodes of the groin. However, it is well to remember that tumor emboli may spread upward into the rectal lymphatics by means of the communications described previously as well as the reverse occurring.

The lymphatic pathways of the vulva have abundant connections with the anal region and the vulva. The usual spread of carcinoma is one that will lead into the iliac and hypogastric nodes. But that there is a connection of lymphatics via the vulva into the inguinal area must be noted. The frequent involvement of inguinal area in lymphogranuloma inguinale adds proof to its presence.

#### INDICATION FOR GROIN DISSECTION

Groin dissection is indicated in metastatic cancers occurring in the inferior extremity, male and female genitals, the perineum, the perianal zone, gluteal region, and the infraumbilical segment of the abdominal wall. There is some question as to whether one should wait for definite evidence such as clinically palpable nodes in cases of epidermoid carcinoma of the extremities. Pack and Hecker (1942) stated that 74 per cent of patients with controlled epidermoid carcinomas of the hands and feet and without palpable regional lymph nodes, subsequently developed nodal metastases while under observation. They suggested that if dissection of these regional lymph nodes had been routinely done on admission, 7 per cent of them would have been unnecessary. However, I believe that even 75 per cent of unnecessary operations in the treatment of an otherwise lethal disease is a small risk.

Dea (1935) stated the experience of the Memorial Hospital in examination of inguinal nodes in epitheliomas of the penis. An error of 14 per cent is made in determining the presence or absence of metastases in inguinal nodes as diagnosed by physical examination alone. At the time of the first examination, in vulval adenopathy is present in about 6 per cent of the patient. Approximately one-half of the nodes were cancerous as proved by biopsy later.

**Lymph Node**—The inguinal nodes, as we employ the term, refers to all lymph nodes in the inguinofemoral region. The glands are arranged as a superficial and a deep group.

The superficial group is arranged as (a) a proximal group parallel the inguinal ligament (superficial inguinal glands) (b) a distal chain on the sides of the long saphenous vein (superficial subinguinal glands).

The chief efferent lymph vessel from the superficial nodes extend either directly into the external iliac lymph nodes above the inguinal ligament or to the deeper inguinal nodes beneath the fascia. These deep lymph nodes are situated laterally and medially to the femoral vein. The highest and most constant of these deep nodes in the femoral triangle is the so-called Cloquet or Rosenmüller's node situated on the medial aspect of the femoral vein at the entrance to the femoral canal or actually within it.

Both the superficial and deep inguinal nodes drain into the external iliac chain, a group of nodes of the periaortic chain. Young called attention to a small node located at the external inguinal ring.

#### REGIONAL LYMPHATIC DRAINAGE

As a rule the lower trunk area drains toward the groin. The upper trunk area drains toward the axillary vessel. The dividing line is usually extended to between the umbilicus and the small of the back.

The lower extremities drain entirely into the inguinal glands. Rarely deeper structures around the gluteal region may drain to the posterior nodes in lymphatics accompanying the gluteal vessel.

There is a very free anastomosis of lymphatic vessel draining the external genitals, and thus bilateral crossed metastasis is common. The main lymphatic drainage from the external genital region is the superficial femoral nodes, chiefly of the superficial external nodal group. From the glans penis and clitoris, deeper lymphatic vessels may pass directly to the deep femoral nodes, or by way of the inguinal canal to the external iliac nodes.

The lymph drainage of the scrotum is remarkably abundant. The collecting lymph vessels originate along the median raphe and anastomose freely with those of the opposite side. On this account the metastases are nearly always bilateral and accordingly bilateral groin dissections are indicated.

The lymphatic drainage of the vulva is very extensive. In Malignancies of this area should eventually therefore have bilateral dissections.

The lymph drainage of the perianal and perineal regions is to the superficial inguinal glands. The extensive intercommunication of both sides of this area is such that bilateral dissection must also be done.

It may be well to insert a word here of the lymphatic drainage of the rectum, anus, and vagina. The latest description of the lymphatic spread of carcinoma of the rectum has been written by Miles (1931) and (1932) (Gleibrist and David (1938) and C. H. Ka and MacIntyre (1940) has contributed much to the up-to-date knowledge of lymphatic spread of colorectal carcinomas.

a review of thirty-eight Bassett operations stated. In spite of many cases of infected wounds, there were no deaths from sepsis. Lewis (1931) in reviewing the results of Young's radical operation for carcinoma of the penis, presented nineteen cases of infection with slough out of a total of thirty-four dissections. Pack and Bekers had an incidence of 96 per cent of badly infected wounds out of a total of 122 groin wounds. Taylor and Nathanson (1942) in their monograph on lymph nodes did not give figures as to wound infection but implied that it occurs with distressing frequency. McKelvey (1947) has suggested that the less undermined skin left in dissection for vulvar carcinoma, the better the primary healing. He practices the wider excision of skin over the inguinal area with primary closure.

The causes of necrosis of the skin have been attributed to various factors: (1) the presence of a large dead space over the femoral triangle following removal of the lymph nodes, fascia and fat; (2) the thin skin flaps; (3) inadequate pressure dressings; (4) the presence of bacteria with lymph nodes from the anus and perineal regions which drain into the inguinal area.

Though these may be factors that are important, it is our impression that careful attention to the fundamental principles of surgical wound healing will obviate this distressing complication. Though it is to be admitted that chemotherapy has aided us materially in cutting down the postoperative morbidity of many surgical procedures, it cannot correct any errors of fundamentals and principles.

#### TECHNIQUE OF GROIN DISSECTION

The patient is placed on the operating table with the corresponding thigh slightly abducted and externally rotated. Any satisfactory anesthetic agent may be used; however, if bilateral dissection is to be carried out, general anesthesia is used.

The skin incision differs from that suggested by Bassett and Taussig. They have suggested a vertical incision. I believe that this type of incision is the cause of the high incidence of wound infection. As was pointed out in the discussion on the blood supply of the skin of the inguinal region, these vessels run in the superficial fascia in a manner parallel to the inguinal ligament. A vertical incision would cut across the blood supply to the medial flap. Our incision, therefore, is about a 14 cm. incision parallel to and about 5 cm. below the inguinal ligament. In its course the middle of the incision is over the palpable femoral artery. Unless the skin is involved, no skin is removed with the specimen.

The incision is then carried down to Camper's fascia, which can be identified as a definite layer by careful traction upward with a fine rake retractor. The small blood vessels can be seen coursing in the fat immediately above skin towels when applied should be clipped with the lightest towel clips possible as heavy manipulation will thrombose the fine vessel to the edges and necrosis will result.

The dissection of the upper flap is then carried out by means of sharp dissection, along Camper's fascia, until a point 2 inches above the inguinal liga-

Colby and Smith pointed out the inadequacy of physical examination alone. In a series of thirty two cases of groin dissection for carcinoma of the penis, eleven of the total were detected although no nodes were palpable. In four or 36.3 per cent, malignant glands were found on microscopic examination.

Groin dissection may be justified as a palliative procedure even when involvement is extensive with beginning necrosis, provided that the disease can be freed from the great vessels. Any procedure which may prevent the necrotic discharging ulcerations in the groin with the attendant infections and hemorrhages constitutes excellent palliation.

The presence of intercommunicating systems of lymphatics between the lower rectum, anus, and vagina, raises a question. Should inguinal node dissection be considered in lesions of the lower rectum and vagina? Gilchrist and David (1948) have shown that 4.6 per cent of tumors of the rectum below the promontory may have retrograde metastases. They have also shown that when a lymph node is destroyed or blocked the lymph drainage is rerouted through collateral channels or by retrograde means, into a channel draining into a normal node.

At the University of Minnesota (Tinic) a careful examination of the inguinal area is made both preoperatively and in the follow-up period in those patients who have had surgery for low rectal lesions. We have come to believe that anal lesions routinely should have an abdominoperineal resection followed by bilateral inguinal node dissections.

Pack and Rekers (1947) enumerated the following postulates for successful groin dissection:

- (1) The primary cancer wherever located should be controlled or controllable and should be treated first.
- (2) There should be no clinical evidence of blood stream metastases.
- (3) The lymph stream must be centrilward without evidence of blockage and retrograde extension.
- (4) It should be technically possible to excise all of the lymph nodes involved as suspected (becoming involved).
- (5) There must be some possibility of interruption of the lymphatic spread of the cancer by an excision of these nodes.
- (6) There should be evidence that the cancer has drained only to the regional groups of nodes to be attacked in the groin dissection.

#### TIME OF DISSECTION

Some surgeons have devised en bloc procedures combining groin dissection with operations on the primary focus of disease (Blumet in 1919, Tausig in 1933 and Young in 1931). In general, however, dissection of the inguinal group of nodes when indicated is carried out as a later procedure two to three weeks after complete control of the primary disease. The groin dissection should not be postponed too long if metastases are clinically evident.

#### ANAL LESIONS FOLLOWING DISSECTION

Following dissection has been reported by Tausig (1933) in

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The incision is then carried down to Camper's fascia, which can be identified as a definite layer by careful traction upward with a fine rake retractor. The small blood vessels can be seen coursing in the fat immediately above. Skin towels when applied should be clipped with the lightest towel clips possible as heavy manipulation will thrombose the vessels to the edges and necrosis will result.

The direction of the upper flap is then fixed out by means of sharp dissection, along Camper's fascia, until a point 6 inches above the inguinal liga-



ment is reached (Fig 1). The dissection then has exposed the anterior superior spine and the external abdominal ring. The scalp is then turned down and the fat and fascia over the external oblique aponeurosis are peeled medially down to the inguinal ligament. At this point the lower skin flap is dissected down to the apex of the femoral triangle. The long saphenous vein is encountered and divided, when the dissection at this point is carried down and through the fascia lata overlying the muscles in this area. The finest 00000 silk (Deknatel) is used throughout except for the larger veins or arteries encountered, for which 0000 silk is used.

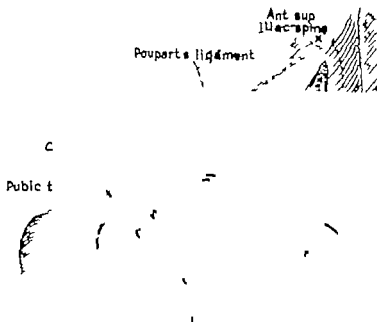


FIG 1—Dissection shows the dissection and early dissection of upper flap. The vertical broken line gives the line of dissection of this flap. Distance is equal. Distance from the inguinal ligament.

Having outlined both skin flaps, the fascia lata is then incised at the lateral border of the sartorius and the medial border of the adductor longus (Fig 2). The dissection is then carried out carefully in a centripetal manner from below upward and from either side inward so that at the end of the procedure the specimen will be attached only by means of the saphenous vein entering the femoral vein (Fig 3).

In dissecting out the femoral vessels, the adcuticular layer of the artery and vein is stripped together with the fat and fascia intervening between these vessels. Near the lower angle of the femoral triangle several small lymphatics may be encountered which should be ligated.

The dissection then is carried from below inward crossing the inguinal ligament toward the saphenous vein. The femoral vessels are then stripped

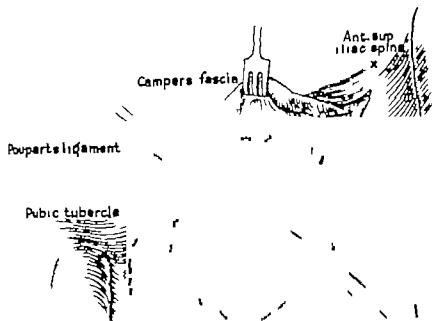


Fig. 3.—Both upper and lower flaps having been outlined the fascia is then incised the lateral border of the rectus abdominis and the medial border of the adductor longus.

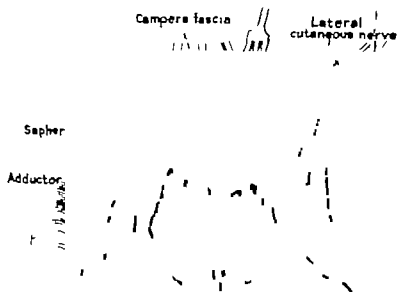


Fig. 4.—The dissection is then carried out carefully to the level of the femoral vein. The end of the procedure will be checked only by means of the superficial vein entering the femoral vein.

ment is reached (Fig 1). The dissection then has exposed the anterior superior spine and the external abdominal ring. The scalpel is then turned downward and the fat and fascia over the external oblique aponeurosis are cleaned meticulously down to the inguinal ligament. At this point the lower skin flap is dissected down to the apex of the femoral triangle. The long saphenous vein is encountered and divided, when the dissection at this point is carried down and through the fascia lata overlying the muscles in this area. The finest 00000 silk (Deknatel) is used throughout except for the larger veins or arteries encountered, for which 0000 silk is used.

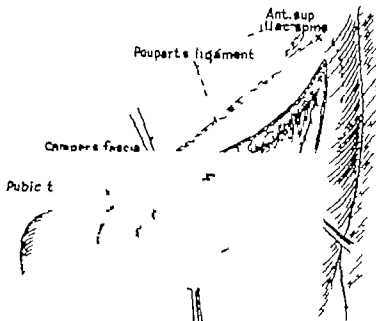


Fig 1.—Illustration shows the incision and early dissection of upper flap. The curved broken line given for limit of dissection of this flap. It extends to point where the femoral vein is encountered.

Having outlined both skin flaps, the fascia lata is then incised at the lateral border of the sartorius and the medial border of the adductor longus (Fig 2). The dissection is then carried out carefully in a centripetal manner from below upward and from either side inward so that at the end of the procedure the specimen will be attached only by means of the saphenous vein entering the femoral vein (Fig 3).

In dissecting out the femoral vessels, the adventitial layer of the artery and vein is stripped together with the fat and fascia intervening between these vessels. Near the lower angle of the femoral triangle several small lymphatics may be encountered which should be ligated.

The dissection then is carried from below downward crossing the ligament femoral toward the saphenous vein. The femoral vessels are again stripped

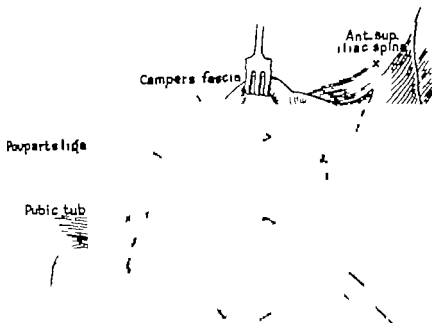


Fig. 2.—Both upper and lower flaps having been outlined the fascia lata is then incised the lateral border of the flaps and the medial border of the ductor longus.

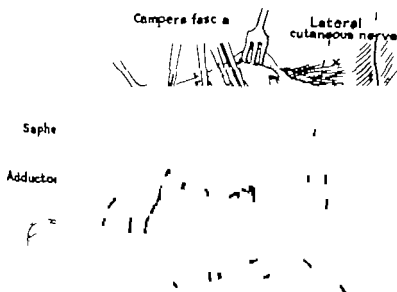


Fig. 3.—The dissection is then tried out carefully in a contraindicated manner from below upward and from either side inward, so that at the end of the procedure the specimen will be attached and by means of the saphenous vein entering the external vein.

ment is reached (Fig 1). The dissection then has exposed the anterior superior spine and the external abdominal ring. The scalpel is then turned downward and the fat and fascia over the external oblique aponeurosis are peeled meticulously down to the inguinal ligament. At this point the lower skin flap is dissected down to the apex of the femoral triangle. The long saphenous vein is encountered and divided, when the dissection at this point is carried down and through the fascia lata overlying the muscles in this area. The finest 00000 silk (Deknatel) is used throughout except for the larger veins or arteries encountered for which 0000 silk is used.

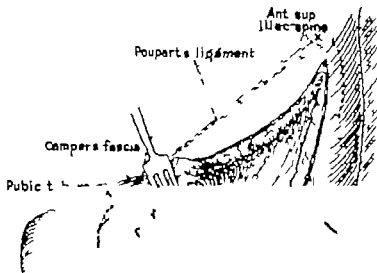


Fig 1.—Illustration shows how the incision and early dissection of upper flap. The curved incision line shows the level of dissection of this flap. 1 shows the point where the incision is made.

Having outlined both skin flaps, the fascia lata is then incised at the lateral border of the sartorius and the medial border of the adductor longus (Fig 2). The dissection is then carried out carefully in a centripetal manner from below upward and from either side inward so that at the end of the procedure the specimen will be attached only by means of the saphenous vein entering the femoral vein (Fig 3).

In dissecting out the femoral vessels, the adventitial layer of the artery and vein is stripped together with the fat and fascia intervening between these vessels. Near the lower angle of the femoral triangle several small lymphatics may be encountered which should be ligated.

The dissection then is carried from below upward crossing the inguinal ligament toward the saphenous vein. The femoral vessels are again stripped

The lateral side of the muscle is then sutured to the iliacus with a series of interrupted sutures. This is repeated on the medial side approximating the sartorius to the adductor longus (Fig 5)

Hemostasis being complete the final stage of the dissection is begun. Fine 00000 silk sutures approximate the undersurface of the skin flaps to the sartorius muscle. These are staggered and are put in so that there is a minimal dead space between the flaps and the underlying muscle. This will also relieve any tension on the skin approximation if some has been removed because of involvement.

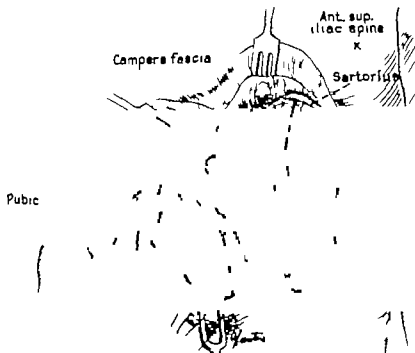


Fig 5  
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This is repeated

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Camper's fascia is then approximated with interrupted fine silk (Fig 6). This maneuver will also prevent any tension on the skin edges. The skin is then approximated with fine epithelial catches which can be left in place for ten to fourteen days (Fig 7).

A light dressing is applied and no drains are used. The patient is kept in bed for twenty-four to forty-eight hours and then allowed to be ambulatory.

#### RESULTS

The procedure described here has been performed on eight patients within the past two years. In one the incision was vertical instead of parallel to the

carefully of adventitia, fat, and fascia. Along the medial side of the femoral vein, the femoral canal is carefully cleaned. The inguinal ligament is retracted upward and the vessels cleaned as far as possible. The spermatic cord should be palpated during the dissection and the fascia overlying it dissected with the specimen.

During the dissection care must be taken to preserve the various cutaneous nerves to the thigh if they are not involved, as an annoying anæsthesia will result.

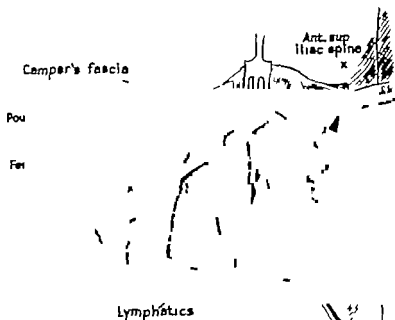


Fig. 4.—Sartorius muscle being cut. Its origin at the anterior superior spine.

Having completely and carefully bared the femoral triangle the sapheous vein is then ligated and cut and the block specimen removed. A triangular defect is thus left around the femoral vessels. This is filled in by means of the following maneuver: a procedure first carried out in this clinic by Owen H. Wangensteen: The sartorius muscle is cut at its origin at the anterior superior spine (Fig. 4). It is then swung over the defect present about the femoral vessels; this transposition of the sartorius muscle suffices to cover the femoral vessels nicely. Fine 0000 silk sutures are then placed between the upper cut end of the muscle and the inguinal ligament above the femoral vessels. Especial care must be observed in suturing the muscle above the femoral canal to prevent a hernia from occurring. Suture of Cooper's ligament to Poupart's ligament is often carried out as a prophylactic measure.

inguinal ligament (Table I). The minimal complications associated with wound slough would indicate the efficacy of this procedure.

#### DISCUSSION

This procedure has not been intended for the group of nodes along the iliac vessels in the pelvis. Though this has been advocated and has been done at times by various surgeons, one questions the advisability. The iliac nodes are enclosed in a variable amount of fat and poorly defined areolar tissue and dissection is not clear. The direct communication of these nodes with the periaortic nodes even as far as the hilum of the lung makes one consider a far more radical procedure such as that of Hunman (1919) for excision of the iliac and periaortic nodes in toto. It is a formidable operation, but perhaps should be considered in selected cases.



Fig. 2.—Photograph of the healed incision, but the line scar that has healed by primary union.

Five of the operations were for carcinomas of the anus or lower rectum. There seemed to be adequate justification for these procedures, in view of the presence of abnormally enlarged nodes in each one of these cases. It must be emphasized again that palpation may be inadequate in discovering metastases, as metastases may be present without palpable lymph nodes, and that consideration to the location of the lesion, pathologic grade and involvement of near-by organs that drain to the inguinal area must be made. With careful pre and postoperative management and the use of careful surgical technique the mortality of inguinal node dissection should be no higher than that of saphenous vein ligation or inguinal node biopsy. The morbidity in this procedure the wound of which heals less kindly than other lymph node dissections and has been due to infection and skin slough, should be almost completely eliminated.





Fig 6—Approximation of Camper's fascia with the #4000 silk suture. This suture will prevent any tension on the skin edges.

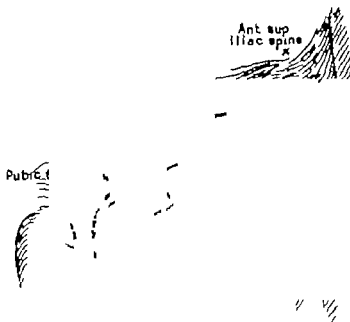


Fig 7—Skin being approximated with the #20 cotton suture. Note the 1/2" to 1" gap for 10 to 14 days.

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An analysis of the cases with reference to the presence or absence of rectum as an influential factor in primary healing of wounds was also made. This has been done because the pertinent suggestion has been made that the cause of poor wound healing in inguinal node dissection is the presence of bacteria

TABLE I. INGUINAL NODE DISSECTIONS

PATIENT	SEX (AGE YR.)	PRIMARY DISEASE	BILATERAL OR UNILATERAL	SKIN SLOUGH	REMARKS
1. L. P.	F 60	Melanoma f foot	Unilateral		Amputation previous
2. V. R.	M 27	Melanoma f foot	Unilateral	-	Furuncul; vertical incision, 150 separated
3. V. V.	M 20	Melanoma f heel	Unilateral	-	Amputation
4. H. M.	M 37	Ca. of sigmoid	Unilateral		Auxiliary dissection th under
5. R. E.	M 61	Ca. f rectum	Unilateral		Abdominoperineal resection
6. M. M.	F 62	Squamous cell	Bilateral		Furuncul separated to rt edema f legs
7. A. K.	M 66	Ca. f rectum	Unilateral	-	Combined abdomino- perineal resection
8. E. C.	M 66	Ca. f rectum	Bilateral	-	Wound, separation on left; find underneath skin margin so slough, healed well

draining from the anus and perianal region. However the analysis showed that there was no significant difference between the two groups. As a matter of fact, the one patient in whom very minimal wound separation occurred had had a combined abdominoperineal resection previously (Case 8). Separations occurred in both groups equally (twice).

A word may be said here as to the use of the antibiotics. Two of the eight patients (both with rectum intact) were given sulfamuxidine preoperatively. The remainder received nothing. One of the two patients receiving the sulfamuxidine did so for twelve days preoperatively and twenty days postoperatively. However in patient thus ignorant therapy a large seroma was present. Radin, Zintel, and Bender (1947) have shown that oral streptomycin is much more effective against all of the common intestinal pathogens than is sulfamuxidine. Perhaps this drug may be indicated preoperatively in certain instances.

Drainage in these procedures can be dispensed with. If the lymphatics at the base of the femoral triangle are ligated with fine silk, the presence of seroma will be avoided. As experience was gained with inguinal node dissection, it was felt more and more that failure to follow this was the main cause of seroma.

## SUMMARY AND CONCLUSIONS

A review of the anatomy of the inguofemoral region is presented. The indications for the procedure of inguinal node dissection are noted. A method of inguinal node dissection is offered which anatomically considers the blood supply of the skin flaps and obliteration of dead space is made. The results suggest that this method is adequate in preventing the common postoperative complication of necrosis and slough of skin.



An analysis of the cases with reference to the presence or absence of rectum as an influential factor in primary healing of wounds was also made. This has been done because the pertinent suggestion has been made that the cause of poor wound healing in inguinal node dissection is the presence of bacteria

TABLE I. INGUINAL NODE DISSECTIONS

IDENT.	SEX (AGE YR.)	PRIMARY DISEASE	BILATERAL OR UNIL. TYP.	SKIN SLOUGH	REMARKS
1 L. F.	F 69	Melanoma of foot	Unilateral	-	Amputation previous
2 V. B.	M 27	Melanoma of foot	Unilateral	-	Seroma; vertical incision, 180 c.s. operated
3 V. V.	M 20	Melanoma of heel	Unilateral	-	Amputation
4 E. M.	M 37	Ca. of sigmoid	Unilateral	-	Anilbry dissection th nodes
5 R. E.	M 61	Ca. of rectum	Unilateral	-	Abdominoperineal resection
6 M. M.	F 62	Squamous cell	Bilateral	-	Seroma aspirated 70 c. rt. edges of legs
A. K.	M 66	Ca. of rectum	Unilateral	-	Combined abdomino- perineal resection
8 E. C.	M 68	Ca. of rectum	Bilateral	-	Wound, separation on left flad underneath skin margins; no slough, healed all

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Drainage in these procedures can be dispensed with. If the lymphatics at the base of the femoral triangle are ligated with fine silk, the presence of seroma will be avoided. As experience was gained with inguinal node dissection, it was felt more and more that failure to follow this was the main cause of seroma.

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A review of the anatomy of the inguino-femoral region is presented. The indications for the procedure of inguinal node dissection are noted. A method of inguinal node dissection is offered in which anatomic consideration of the blood supply of the skin flaps and obliteration of dead space is made. The results suggest that this method is adequate in preventing the common postoperative complication of necrosis and slough of skin.

by the kidneys. The choice of glucose solution because normal saline is ineffective cannot be logically—or physiologically—defended. It is frequently unrecognized that although sodium salts are confined chiefly to the extracellular fluid, to raise the sodium concentration in this fluid by a given increment it is necessary to give enough sodium to increase its concentration in the total fluid of the body (both extracellular and intracellular) by this amount. This follows from the fact that the cell membranes are freely permeable to water. When the osmotic pressure of the extracellular water is raised by the addition of salt enough water passes from cells to extracellular fluid to restore osmotic equilibrium between the two compartments.

Assume a patient with a total fluid volume of 60 liters, of which 20 is extracellular and assume that this extracellular fluid contains 120 millimols per liter of sodium instead of the normal 137. To raise this concentration from 120 to 137 millimol in the extracellular fluid alone would require  $15 \times 20 = 300$  millimols of sodium. However since there would be the transfer of water mentioned previously the amount actually required would be  $15 \times 60 = 900$  millimols of Na. This is approximately the quantity found in 6 liters of normal saline solution, containing 150 millimol per liter. To secure the desired effect however the salt would have to be introduced in the dry form. Introduction of 6 liters of 150 millimolar saline solution would increase the sodium concentration of 60 liters of fluid from 120 millimolar only to 123 millimolar. To raise the concentration from 120 to 137 millimols with normal saline solution would require 60 liters of fluid. It is clear from these calculations why Coller and his associates increased only the edema without raising the serum sodium in their patients by injections of normal saline solution. Their failure did not justify the inference that sodium chloride is contraindicated in the treatment of edema with hyponatremia. It was not the salt that was at fault, but the large amount of water in which it was dissolved. Normal saline solution in proper quantities is appropriate for the maintenance of patients in a state of adequate hydration with normal serum electrolyte patterns. It is the fluid of choice for patients who are dehydrated. But for the correction of serum sodium deficit in the presence of an adequate supply of fluid or edema, hypertonic (3 to 5 per cent) salt solution should be given. By this means the introduction of large volumes of fluid can be avoided. If the heart is competent, such treatment, by increasing the circulatory insufficiency that accompanies hyponatremia, will promote diuresis and elimination of the edema. It may be supplemented by glucose solution but again the glucose should be given in concentrated form (10 per cent). It is objected that hypertonic solutions are likely to cause venous thromboses. This can be avoided if care is taken to preserve a free flow of blood in the vein by the use of a small needle so inserted and fixed that there is no obstruction to blood from the more distal part of the vein. It should be unnecessary to add that it is futile to inject salt solution of any concentration if precautions are not taken to prevent wastage of salt by other channels. Transfusions and other measures for the support of the circulation must not be neglected.

# Editorial

## The Treatment of Salt Depletion

FROM the standpoint of the bodily economy it is important that the electrolyte osmotic pressure and reaction of the extracellular fluids be maintained within normal limits—that is, that the concentrations of sodium, chloride and bicarbonate in these fluids all be kept at an optimum. The sodium in the extracellular fluid controls the distribution of water within the body. If its concentration falls below normal, the cells of the tissues take up water and swell, just as red blood cells do in a hypotonic solution. This leads to certain secondary disorders, the chief of which is circulatory failure.<sup>1,2</sup> This conduces to impairment of renal function and delay in the excretion of water as well as sodium salts. Consequently patients with such a condition may develop edema, even when the concentration of sodium salts in the serum and extracellular fluids is low. The tendency to edema is aggravated by concomitant hypoproteinemia which may result from malnutrition or severe injury.

Such a condition of edema with hypoproteinemia and hyponatremia is most frequently encountered in patients who, having become depleted of salt by vomiting or diarrhea, are given fluids without salt to overcome the dehydration. Patients commonly present themselves for treatment in this state. Unhappily some are still reduced to this condition by misdirected therapeutic measures. Vomiting patients are given water or other fluids without salt to drink. Water instead of normal saline solution, is used for lavage or irrigation of the gastrointestinal tract. Glucose solutions alone or with inadequate amounts of saline solution are given intravenously. One of the commonest causes of salt depletion and edema is the lower nephron nephrosis produced by crush injuries, hemolytic transfusion reactions, and poisoning from a variety of drugs including the sulfonamides. The salt depletion in these conditions presumably arises chiefly from initial vomiting and is often exaggerated by a tedious dehydration. When the nephrosis is established failure of tubular reabsorption and consequent leakage of salt into the urine may contribute to it.

Obviously the first consideration is the avoidance or prevention of the circumstances which produce salt depletion. The second is to include adequate amounts of salt in the fluids given to overcome dehydration. There will still remain the problem of treating a certain number of patients with edema and low serum sodium and chloride. Colle and his associates<sup>3</sup> have pointed out that administration of normal saline solution to such patients exaggerates the edema without restoring the concentration of sodium salt. The total quantity of such salts in the body may even be decreased. They therefore advocate the use of nothing but small amounts of glucose solution. This procedure fails, however, to rectify the deficient concentration of sodium which, because of its effect upon the circulatory state is partly responsible for the defective elimination of water.

by the kidneys. The choice of glucose solution because normal saline is ineffective cannot be logically—or physiologically—defended. It is frequently unrecognized that, although sodium salts are confined chiefly to the extracellular fluid, to raise the sodium concentration in this fluid by a given increment it is necessary to give enough sodium to increase its concentration in the total fluid of the body (both extracellular and intracellular) by this amount. This follows from the fact that the cell membranes are freely permeable to water. When the osmotic pressure of the extracellular water is raised by the addition of salt enough water passes from cells to extracellular fluid to restore osmotic equilibrium between the two compartments.

Assume a patient with a total fluid volume of 60 liters, of which 20 is extracellular and assume that this extracellular fluid contains 170 millimols per liter of sodium, instead of the normal 135. To raise this concentration from 120 to 135 millimols in the extracellular fluid alone would require  $15 \times 20 = 300$  millimols of sodium. However since there would be the transfer of water mentioned previously the amount actually required would be  $1 \times 60 = 600$  millimols of Na. This is approximately the quantity found in 6 liters of normal saline solution containing 100 millimols per liter. To secure the desired effect, however the salt would have to be introduced in the dry form. Introduction of 6 liters of 135 millimolar saline solution would increase the sodium concentration of 60 liters of fluid from 120 millimolar only to 123 millimolar. To raise the concentration from 170 to 135 millimols with normal saline solution would require 60 liters of fluid. It is clear from these calculations why Coller and his associates increased only the edema without raising the serum sodium in their patient by injections of normal saline solution. Their failure did not justify the inference that sodium chloride is contraindicated in the treatment of edema with hyponatremia. It was not the salt that was at fault but the large amounts of water in which it was dissolved. Normal saline solution in proper quantities is appropriate for the maintenance of patients in a state of adequate hydration with normal serum electrolyte patterns. It is the fluid of choice for patients who are dehydrated. But for the correction of serum sodium deficit in the presence of an adequate supply of fluid or edema, hypertonic (3 to 6 per cent) salt solution should be given. By this means the introduction of large volumes of fluid can be avoided. If the heart is competent, such treatment, by overcoming the circulatory insufficiency that accompanies hyponatremia, will promote diuresis and elimination of the edema. It may be supplemented by glucose solution but again the glucose should be given in concentrated form (10 per cent). It is objected that hypertonic solutions are likely to cause venous thrombosis. This can be avoided if care is taken to preserve a free flow of blood in the vein by the use of a small needle so inserted and fixed that there is no obstruction to blood from the more distal part of the vein. It should be unnecessary to add that it is futile to inject salt solution of any concentration if precaution are not taken to prevent wastage of salt by other channels. Transfusions and other measures for the support of the circulation must not be neglected.



Proper regulation of the salt intake, especially when hypertonic solutions are employed, should be controlled by frequent analyses of the serum. Until suitable flame photometers become available, it will be necessary to estimate sodium by inference from the concentrations of bicarbonate and chloride. Inclusion of sodium will permit more precise regulation.

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—John P. Peters, M.D.  
 Ken H. van, Conn

# Recent Advances in Surgery

COMPILED BY ALFRED BLALOCK, M.D.

## HEMORRHAGE INTO THE BILIARY TRACT FOLLOWING TRAUMA— TRAUMATIC HEMOBILIA

PHILIP SANDSTRÖM M.D. M.B. STOCKHOLM SWEDEN

(From the Surgical Department of the Örebro Hospital)

**H**EMORRHAGE into the biliary ducts as a result of trauma to the liver region has previously been observed only in rare cases. With reference to one of these Wright and associates<sup>1</sup> mentioned that in central rupture of the liver blood, because of its entrance into the biliary tract, may appear in the vomitus. In his comprehensive monograph on injuries to the liver and biliary ducts, Thole<sup>2</sup> discussed the matter with the following sentence: "Bloody stools are a very rare early symptom, and only those are of interest in this connection." Other authors as Andersson, Bauer, Brandberg, Castrén, and Vance<sup>3</sup> do not even mention the condition which would thus appear to be very rare.

The object of this work is to study the symptom of hemorrhage into the biliary tract its frequency and its character. It will be based on a critical review of the literature. The subject was brought up by the following case observed in the Örebro Hospital.

**CASE 1** (Örebro Hospital, N. 2474/1936).—A previously healthy boy 7 years of age, was admitted to the surgical service. Ten days prior to admission he had while bicycling received a hard blow from the handle bar over the right lower part of the chest. He immediately felt severe pain at the site of the blow and became very pale. These symptoms lasted about thirty minutes. Some hours later he again had severe pains in the right flank, and pallor. He was examined at the Dispensary and bruise was found at the site of the blow but nothing pathologic was observed. Two days later there renewed spontaneous cramping in the right flank, and chills. Afterward he was confined to bed with an evening temperature of about 38.5 C. He had cough during the first week. Ten days after the trauma there was renewed, rather severe colicky pain in the right flank and, in addition, marked pallor and jaundice. He was referred to the hospital.

**Examination.**—The general condition was good. He was febrile, had slight anemia with 60 per cent hemoglobin, red cell count 3,000,000 but cell count 12,000 sedimentation rate 23. Urinalysis revealed urobilinogen reaction negative urobilin markedly positive. The abdomen was soft and not distended. The right flank was tender. At the right lateral rectus border immediately below the thorax there was a rounded mass the size of a pigeon egg. Roentgen examination of abdomen, chest and colon showed nothing pathologic. It was considered likely that the patient had retroperitoneal hematoma. This opinion was supported by the well defined tenderness of the right flank with absence of symptoms from the rest of the abdomen, and by the anemia and the leukocytosis. In the evening the patient again had severe pains at this site.

**Operation.**—Cholecystectomy and drainage were carried out. Incision was made at the right lateral rectus border above the umbilicus. Liver, gallbladder, and bowel had normal

\*Operation performed by Professor O. Johansson, surgeon-in-chief.



Siegel assumed the course to be as follows: The blow from the handle bar in addition to the fracture of the ribs and the rupture of the liver caused a contusion of the gall bladder. In consequence of this contusion a hemorrhage to the gall bladder occurred. On the eighth day a blood clot occluded the cystic duct and gave rise to the severe attack of pain in the same manner as the passage of a stone. When the coagulum had passed and had been evacuated per rectum there appeared a temporary improvement. A renewed impaction of a coagulum occurred and infection from the bowel supervened, whereby the conditions prerequisite for distention gangrene arose.

The rarity of such a course was ascribed by Siegel to the fact that the trauma must be accurately balanced—a slighter trauma does no damage and a more severe trauma causes total rupture of the gall bladder. Siegel pointed out that the case is of particular interest in that it shows that a blood clot may have the same sequelae as a gallstone: colicky pain, inflammation, and gangrene.

*Comment*—The history of the present case (Case 1) and that of Siegel (Case 2) were very similar—even the trauma was identical. In the case of Siegel, however, the gall bladder was gangrenous by the time of the operation. As to the cause of the gangrene it could either be a direct effect of the trauma or more likely the effect of distention of the gall bladder caused by an impaction of coagula.

#### DISCUSSION

It was in both instances considered that the hemorrhage emanated from a lesion in the mucosa of the gall bladder.

According to my opinion, however, this is not certain. The blood may also have come from a *central rupture of the liver* and have been carried to the gall bladder through the biliary duct. This hypothesis is supported by the following fact. In Case 1 no source of the hemorrhage was found at inspection of the interior of the gall bladder. In Case 2 the gangrenous part of the gall bladder which was supposed to have been the source of hemorrhage was situated in the fundus where the blood vessels are smaller than in any other part of the gall bladder. On the whole it is unlikely that the small vessels of the gall bladder or the external bile ducts which might be concerned would give rise to such profuse and protracted bleeding. In the thirty odd cases of total rupture of the gall bladder or the external bile ducts reported in the literature the bleeding has in all instances been insignificant provided that there has not been concomitant damage to the liver (Rudberg,<sup>22</sup> Norgore,<sup>23</sup> and Lewerentz).

In Case 1 it appears as though the bleeding had continued after the removal of the gall bladder because blood emptied through the wound two weeks later. This blood may of course also have come from a hematoma in the operative region but the simultaneous obstruction of the hepatic duct makes it more probable that it emanated from the liver.

A central rupture of the liver would satisfactorily explain the protracted hemorrhage as the thin walled vessels of the liver parenchyma have but slight power of contraction. The external ruptures found by Siegel on the lower

appearance. There was no peritonitis, and no free blood in the abdomen. The gall bladder was distended, glistening blue and firm. It could not be evacuated by means of slight compression. Dark brown blood was obtained on puncture. The gall bladder however could not be aspirated by this measure, wherefore it was incised. Its contents of coagulated firm blood clot the mass of hemorrhage was removed. The source of the hemorrhage was found in the gall bladder. This was sutured and the abdomen was closed.

The wound healed without complications. During the first days after the operation Weber's test for blood in feces was markedly positive but six days later it was negative. After one week the patient was discharged free from discomfort. Three weeks later he was reported entirely well with absence of symptoms. Repeated tests for blood in the stools during this period were negative. Twelve years later it is reported that the patient had no discomfort from the operation and never had any discomfort from the liver or the biliary ducts.

*Comment*—As a result of the distinct trauma toward the hepatic region there occurred in this case a hemorrhage into the biliary tract. At operation performed ten days after the trauma liquid and coagulated blood were found in the gall bladder. No source of the hemorrhage could be observed, however. In the further course blood was for some time demonstrated in the stools.

The symptoms that occurred may be explained by this hemorrhage. The pallor and yawning were the expressions of a slight shock and a moderate secondary anemia. The pyrexia may have been caused by resorption of the blood. The attacks of pain, which had the character of biliary colic, were probably brought about by the presence of coagula in the biliary tract.

Before entering upon the discussion of the source of the hemorrhage I wish to describe a case, very similar to the present one, reported by Sargel<sup>18</sup> in 1909

Case 2—A 32 year old man on a bicycle fell with his right side against the handle bar. He immediately felt severe pain. The site of the blow but was able to get home unassisted. A physician found multiple fractures of the ribs on the right side and blood in the right pleural cavity. Soon the patient felt better but on the eighth day he had severe attacks of abdominal pain which were not relieved by large doses of morphine and opium. Not until the tenth day had long coagula was passed per rectum, was the distress relieved. On the twelfth day there was renewed abdominal pain and temperature of 38° C. On the fourteenth day there was condition of collapse with renewed severe colicky pain.

At examination the patient was found to be slightly sclerotic. Marked dilation on the right side of the level of the aorta merged over into the liver dilation which reached down to the atriocaval space. Below the hepatic dilation some palpated. On puncture of the right pleura a small amount of blood was obtained. The lung was emphysematous already at the depth of 8 cm.

Operation.—At laparotomy small amount of blood was found in the abdomen. The gall bladder was enveloped in the omentum. When this was lowered the gall

escaped from the gall bladder. The gall bladder as extracted was on the surface of the liver and measured up to the length of 4 cm. A drainage tube was inserted into the bladder.

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wound took 1 pain and 1 dry 1 for

he was quite historic.  
A few of his friends from the second batch had commenced work. They the others were  
ceased at the beginning of the attack. I paid. It was assumed that I had not been  
the way but the hepatitis and the common duct, giving rise to bile stasis. It possible  
the patient recovered entirely. About further measures

and bleed through a large biliary duct until healing finally occurred. He could not give any other explanation for the continued bleeding through the biliary channels.

*Comment*—Case 3 is so similar to Cases 1 and 2 that it seems highly probable that they have the same cause. In Case 3, however, the hemorrhage certainly could not have come from the gall bladder as it continued for week after cholecystectomy. It must have come from the interior of the liver.

In all likelihood the three cases demonstrate the effect of hemorrhage into the biliary tract originating from a central rupture of the liver. Before discussing the different aspects of the symptom a short account will be given of this special type of injury.

#### CENTRAL RUPTURE OF THE LIVER

Liver lesions may be divided into the following groups (Brandberg):

##### 1 Ruptures through the capsule and the parenchyma

Subcapsular lesions

(a) Subcapsular hematoma

(b) Subcapsular rupture

(c) Central rupture (term introduced by Wilms<sup>21</sup>)

Kroenke<sup>22</sup> suggested and Hamalainen<sup>23</sup> proved in experiments that most central ruptures of the liver are caused by compression of the delicate and fragile liver parenchyma. A tear occurs, veins and bile ducts rupture, and a cavity filled with blood and bile is formed.

By careful examination of a series of autopsies, Bauer<sup>2</sup> could show that central ruptures of the liver are not infrequent—they probably occur at least as often as ruptures through the capsule. Because of their location in the interior of the liver they do not give rise to the hemorrhage and bile leakage into the peritoneal cavity which generally is such an alarming symptom of ruptures through the capsule. While the liver capsule is very sensitive the parenchyma itself has few sensory nerves.

Those are the reasons why central ruptures give such vague symptoms, if indeed any at all and therefore often escape diagnosis. Some of them may heal with scar formation without complications, others produce cavities filled with blood and bile and may later give rise to liver abscesses.

Symptoms of central liver ruptures may appear early or late (Anderson).

##### Early symptoms

1 *Contusion* of the wall of the chest or the abdomen.

<sup>a</sup> Shock

Those two symptoms of course are unspecific.

3 *Pain*. Most authors agree that true central ruptures are painless unless a hematoma is produced sizeable enough to enlarge the liver. A dull aching pain radiating through the shoulders, generally the right one is then a sign of the tension of the capsule. If the cavity breaks through to the capsule the pain becomes more intense.

surface of the liver are similar to those frequently found by Hamalinen<sup>14</sup> concomitantly with central ruptures.

On the basis of this line of argument I consider it highly probable that the hemorrhage in the two cases described arose from a central rupture of the liver. The following very interesting case reported by Hawthorne and associates, from the American Hospital for Disease of the Stomach, not only supports this conclusion but also throws considerable light on the whole subject.

CASE 3 (No 21454).—I 1941, a truck run blew off striking the anterolateral chest wall, upper abdomen, and face of man. He was given much treatment for shock, fractured seventh and eighth ribs, and fractured nose. The injury to the thoracic cage masked the intra-abdominal injury so that it was not recognized at this time in spite of heartlessness on two occasions and tarry stools which were noticed by the patient. After seven days of hospitalization he was discharged and returned to work some weeks after the date of injury. Two weeks later while at work he felt sudden pains of suffocation in the upper abdomen but most marked in the gall bladder area. He vomited large amount of blood and there was gross blood in the stool.

Upon admission, fourteen weeks after the injury the red cells were 3,750,000 and the hemoglobin 47 per cent. All physical findings were negative. By the use of blood transfusions and intravenous glucose he improved to the extent that the red cell count was 4,150,000 and hemoglobin 70 per cent. During this time however he vomited on three occasions very thick black material which on examination proved to be mixture of blood and bile. The patient was allowed to go home two months after admission, still showing traces of occult blood in the stool.

He was readmitted to the hospital three weeks later and plainly showed the effects of a severe hemorrhage the night before. During the three weeks at home he had several attacks, consisting of sense of tightness in the upper abdomen and severe colicky pain followed by nausea and vomiting of the same thick black material that had been vomited in the hospital. He also passed this same type of material by bowel. A large defect in the posterior end of the stomach was demonstrated by x-ray examination.

Operation.—A upper right rectus incision revealed a mass of adhesions over the gall bladder and duodenal areas. After was demonstrable, but in view of the large amount of hematoma it was deemed advisable to open the duodenum. The mesal flexure of duodenum was wide. No definite ulcerated areas were found, but several small congested areas in the mucosa were touched with the cautery and the incision was closed transversely. This did not explain the bleeding and, on releasing the duodenal adhesions the gall bladder

was found to be very dark in color to be enlarged, and to contain a smooth hard mass the size of an egg. The gall bladder was removed and the bile ducts were explored through the papillary cystic duct. Some very dark material of the same type that he had vomited was found, but there was no evidence of tear of the duct or liver. The large mass in the gall bladder proved to be impure blood and bile.

He made an uneventful postoperative recovery and was discharged on the nineteenth day. The stool was negative for occult blood.

One week later he had another attack of colicky pain in the subhepatic area lasting one hour and vomiting small amount of the very dark material that had been observed on previous occasions. A large amount of green black fluid was passed by bowel. There followed

the best that  
could be given  
entirely free of

Hawthorne concluded that in all probability there was in this case a cavity and hematoma deep in the substance of the liver that continued to necrose

The three cases described give examples of all these happenings. In Case 3 there was blood in the vomit and all three patients had blood in the stools. There was marked biliary colic in all three and in Case 2 there was transitory jaundice.

# REVIEW OF CASES

The cases of subcapsular liver lesions reported in the literature have been examined with special attention to symptoms suggesting hemobilia. This has met with the following difficulties:

1. The case histories are often incomplete and give too scanty information on the necessary points. Some cases with hemobilia might therefore escape recognition.

The symptoms when found can often be due to other causes than hemobilia. In fact most authors have given other explanations. Bloody vomit and stools may be caused by concomitant lesions of the digestive tract or by swallowed blood. Pain may emanate from a capsule in a state of tension or irritation. Jaundice may be due to resorption of bile from a cavity in the liver etc.

3. The diagnosis of central liver rupture is often uncertain especially if operation or autopsy has not been performed. Even after operation it is often difficult to decide whether it is a case of true central rupture or subcapsular lesion.

I have found forty cases where with different degrees of probability a central rupture of the liver occurred. In nine of these the patient died on the first day and in another two within the first four days.<sup>2, 4, 5, 20, 21, 22</sup> In nine others the information is too scanty to allow any estimation.<sup>1, 2, 3, 23, 24, 25</sup> This leaves twenty cases where the problem in question may be studied. In eleven cases no signs of hemobilia are described.<sup>2, 2, 12, 22-27, 31</sup> (In five of these however there are reasons to believe that the lesion was subcapsular.<sup>2, 23, 29</sup>) In the remaining nine cases there were signs indicating a hemorrhage into the biliary tract. Three of them were reported herein as Cases 1 to 3. The rest of these cases have been divided into groups according to which main sign of hemobilia they present: hemorrhage or biliary colic.

*Cases With Hemorrhage*—Cases 4 to 6 (also Cases 1 to 3) had hemorrhage. Case 4 was reported by Owen<sup>23</sup> in 1848.

CASE 4—A man 22 years of age fell from a wagon. He had an immediate state of shock and complained of pain in the stomach. Even two hours later he was then in deep shock. There were no signs of injury on the trunk. The next morning he was better but complained of pain in the right shoulder which was not damaged. He had pressure over the region of the liver extending up the back of the chest. He was short of breath and could lie only on the left side. When he tried to turn the pain became worse especially in the shoulder.

The third day the attacks of pain were less. There was some jaundice. On the fourth day he had paroxysms of pain two or three times, but not so much pain on pressure over the abdomen. The jaundice had increased.



#### 4. Signs of bile in the blood and the urine

A bradycardia caused by bile salts in the blood seems to be a rather uncertain symptom. Finsterer<sup>2</sup> stressed the importance of this symptom but later authors as Wright and associates<sup>21</sup> have not been able to find it.

Jaundice may be caused by the resorption of bile from the cavity or may be the result of an obstruction of the biliary ducts. Castrén<sup>2</sup> has demonstrated the presence of leucine crystals in the urine.

5 Enlargement of the liver is dependent on the size of the cavity formed.

6 Secondary anemia seldom becomes pronounced.

7 Embolism to the heart and lungs is a serious complication in some cases. It is caused either by pieces of liver tissue or fat from the liver cells which enter the circulation via the hepatic veins.

#### Late symptoms

An enlargement of the liver and also jaundice may appear some time after the lesion.

8 Fever is generally a sign of resorption from the intrahepatic hematoma. It can also be a sign of infection in the cavity with the formation of an abscess. Liver abscesses often are sequelae of intrahepatic hematomas.

#### HEMOBILIA

If the essential cause in the three cases described was a central rupture of the liver which seems highly probable the list of symptoms of this type of injury could be supplemented with that of hemorrhage into the biliary tract. This symptom may be compared to the hematuria which results from damage to the kidneys and accordingly termed hemobilia.

Hemobilia might be expected in all types of liver injuries, but it should be more prominent in the central ruptures for the following reasons:

1 Patients with ruptures through the capsule generally lie or get treated so short a time after the trauma that a hemobilia would not make itself evident. When the capsule is torn, there will be less resistance to the blood flow into the peritoneal cavity than into the biliary tract.

In central ruptures more and larger biliary ducts are apt to tear than in superficial ones. This will facilitate the escape of blood into the biliary tract. In subcapsular hematomas there might not be any lesion of the biliary tract at all. It is suggestive that most of the cavities formed by this type of lesion contain blood without bile.

Whereas a hematuria, at least when macroscopic, is a very striking symptom, a hemobilia is apt to be overlooked if it is not so profuse that it causes bloody vomit or tarry stools.

In the course of hematuria the formation of blood clot usually gives more alarming symptoms of urinary colic or obstruction. The same should be expected in the biliary tract where clots would cause biliary colic and even finally obstruct the duct with risk of jaundice. It should be remembered that the bil has an inhibitory effect on the clotting of blood, which should increase the number of cases with this complication.

The source of the copious melena could hardly have been the epistaxis which is not described as being serious. There was no hematemesis and the blood did not show signs of having been digested in the stomach. As there was no other lesion in the digestive tract the blood probably originated in the liver.

Owen himself discussed the connection between the melena and the improvement of the patient, characterized by the disappearance of the hiccups, the decrease of jaundice, the diminished pain, and the reduction in size of the liver. As he thought that there probably was a connection he looked for a direct communication between the cavity in the liver and the intestines.

With the experience gained from Cases 1 to 3 there does not seem to be much doubt that the communication which Owen looked for in vain was the biliary tract and that the melena was a sign of hemobilia.

Hitzrot reported the following case from The New York Hospital in 1908.

Case 3—A man aged 33 years admitted. He complained of swelling in the upper part of the abdomen, distress, pain in the abdomen radiating to the left side and at the back below the left shoulder blade and blood in the stool.

Four months before admission the patient had been struck, while at work, a severe blow upon the stomach by a truck at 7. Following the blow he was nauseated, felt weak, and had severe abdominal pain for which he consumed large quantities of whiskey. He was unable to work as the pain was aggravated by moving, coughing, vomiting, or deep breathing. About ten months after the injury the pain became more intense, as localized definitely to the epigastrium, and the patient could neither lie down nor sleep. About three months after the injury a swelling appeared which thereafter gradually increased in size. Throughout, he had morning vomiting which never contained blood.

Examination.—The general examination was negative. The abdomen was markedly swollen in the epigastric region, where there was a large tender mass extending from the costal margin almost to the navel and laterally about six inches each side of the median line. The mass seemed of the semispherical, and quite superficial. It was continuous with the liver dulness. The stools contained blood once. Hemoglobin was 7 per cent. The temperature ranged from 90 to 101 F.

Operation.—A median epigastric incision was made over the center of the mass, exposing a large cystic mass projecting from the liver surface. On aspiration with a trocar 8 ounces fluid blood were obtained, the removal of which left a large cavity which extended deeply into the surface of the liver. This cavity was packed with two large one-pound gauze rolls. The other viscera felt normal. Convalescence uneventful and the patient was discharged from the hospital at the end of six weeks. Four months after the operation he was reported as free from pain. Stools were normal and he again resumed work.

Hitzrot comments. This case presents many features of interest, namely the long period of symptoms, the gradual appearance of the swelling, the marked alcoholic history, the size of the blood cyst and the long period (five months) which elapsed between the injury and the operation.

The case represents the type of subcapsular hematoma of some size forming a blood cyst.

Comment.—There was probably a subcapsular rupture in this case which produced a subcapsular cavity through a gradually increasing collection of blood. As in the preceding cases the pain was of the kind that usually emanates from the capsule.

The symptom of blood stools is just mentioned, but it seems to have been one of the chief complaints of the patient when he entered the hospital four

On the sixth and seventh days, the stools contained mucus and bright blood. The jaundice was increasing. He got troublesome hiccups which continued on the eighth day. Epistaxis occurred 1 or three times. In the evening of that day he passed mucus consisting of nearly one half pint of dark grumous blood.

Even on the sixth day the mucus consisted of dark colored bloody siala. There was no more hiccup. The jaundice was decidedly less. The countenance was cheerful. There was no pain and the dullness over liver did not extend very high. A favorable prognosis was given.

On the tenth and eleventh day there was very little mucus. The face looked puffed, the pulse was easily compressed and the abdomen was distended.

On the twelfth day he was delirious. Hands and thumbs were twitching. In the afternoon while his head was being raised he as relaxed all general contractions and ceased to breathe within five minutes.

*A autopsy.*—There was no blood in the peritoneal cavity. There was no peritonitis. The liver was much enlarged and there were some soft abscesses between its convex surface and the diaphragm. When taken out, a laceration was seen extending across its right lobe. At the back of the laceration, which extended deeply into the lobe there was a collection of fluid and clotted blood. No connection between this and the intestines as found. No other lesions of any importance were discovered.

Owen discussed the case at length. Only his comments on the hiccups and the melena will be related.

The hiccup, another not unusual symptom of affections especially of the diaphragmatic surface of the liver did not appear until about the sixth day after the injury and although severe and urgent while it lasted, was not of long continuance. Did this symptom, so firm an accompaniment of inflammatory action about the surface of the diaphragm and liver mark the period of formation of the soft adhesions found connecting the diaphragm and liver? Did it depend on some temporary increase of upward pressure only and become relieved by the evacuation of the grumous blood as it began to disappear here this took place?

Although probably the mucous-mucous discharges from the bowels were chiefly due to the remedies employed, yet from the facility with which they were brought on, and the frequent attacks of epistaxis, there probably existed more or less congested state of the mucous membrane throughout in regard to the large discharge of blood on the evening of the eighth day viewing as I then did, the case as one of general congestion, with congested state of liver I had hoped it could have proved a salutary or critical discharge for it will be noted that not only the hiccup, until then distressing, ceased about this time, but the countenance and manner became

undisturbed, and the

regurgitated from the portal  
relieved or removed the congested state of liver

*Comment.*—Owen's case was admirably well studied and commented. It is regrettable that space does not allow it to be related in full.

The death in his case was probably caused by shock due to the liver injury and secondary anemia. The type of pain with irradiation through the right shoulder and with relief when lying on the left side is typical of a lesion close to the capsule. The paroxysms of pain on the fourth day when there was not much pain on pressure over the abdomen could have been caused by blood clots in the biliary tract.

intestinal and solitary ones in both kidney pelvis. These were supposed to be of toxic origin. Another possibility is that they were caused by the sudden increase in the venous pressure when the thorax was compressed.

The blood in the vomit and in the stools could have originated from these hemorrhages in the mucosa. Considering the large amounts of blood that were lost and with the experience gained from Cases 2 and 3 it seems more likely that the blood came from the liver lesion. The changes in volume of the liver that are described could have been due to evacuation of blood through the ducts alternating with hemorrhage from the wall of the cavity.

**Cases With Biliary Colic**—Cases 5 to 9 (also Cases 1 to 4) had biliary colic. Such a case was reported by Holm<sup>13</sup> at the Surgical Department of Geh. Rat Bkr in Berlin in 1914.

**CASE 7**—A 19-year-old laborer was admitted after having been run over by an automobile while bicycling. He was in great distress on admission. He had fracture of the left forearm and also an extraperitoneal rupture of the bladder which was operated upon.

After an improvement of a few days he suddenly had an intense pain below the right costal margin, radiating to the right shoulder. On examination he was found to have a distended abdomen. The liver was enlarged to twice the normal size and the consistency distended like a balloon (the biliary ducts are not described). Upon puncture of the liver cavity was found about 1000 c.c. more than 1 cm. thick liver of peritoneum. From this 2 liters of fluid consisting of bile and blood, were aspirated, after which the liver collapsed. The cavity was drained. In the beginning there was abundant secretion but six weeks later the wound was healed. The patient recovered.

Two weeks after the accident his condition became worse. He became lethargic and had violent attacks of vomiting. The liver region remained just as tender but it was also noted that the liver was markedly enlarged.

**Operation**—Operation was then carried out. There was no blood in the abdominal cavity and no peritonitis. The liver was enlarged to twice the normal size and the consistency distended like a balloon (the biliary ducts are not described). Upon puncture of the liver cavity was found about 1000 c.c. more than 1 cm. thick liver of peritoneum. From this 2 liters of fluid consisting of bile and blood, were aspirated, after which the liver collapsed. The cavity was drained. In the beginning there was abundant secretion but six weeks later the wound was healed. The patient recovered.

Holm concluded that this was a case of central rupture of the liver, noteworthy because of the unusual amount of bile mixed with blood that was found in the cavity.

**Comment**—In this case there was undoubtedly a central rupture of the liver with an accumulation of bile and blood. The severe pains below the right costal margin radiating to the right shoulder had a definite character of biliary colic. They can hardly be explained by the swelling of the liver with distention of the capsule as the abdomen then was entirely soft and not tender. The tenderness did not appear until after several days, and the signs of hepatic enlargement appeared still later. The course of this case is best explained by the presence of blood clots in the biliary tract.

The following case was reported by Hranberg<sup>14</sup> from the Lund Hospital in 1906.

**CASE 8 (N. 2047)**—A boy aged 14 years was knocked down by a horse and was hospitalized on the following day. On admission right-sided fracture of the sternum was established and was treated upon. There was some tenderness in the right side of the abdomen from the navel up into the epigastrium. There was a fracture of the pelvis and

months after the accident. During his hospital stay the stools contained blood once. The protracted hemorrhage can in this case best be explained as caused by the liver lesion.

The following case was reported by Wulsten<sup>22</sup> from The Surgical Department of the Hindenburg Hospital in Berlin in 1931

**CASE 6**—An 11 year old girl was admitted to the hospital

**History**—Four weeks before admission while she was coasting, her sled had run into fence. She received severe blow in the upper abdominal region. She began to vomit and complained of severe pain in the whole body. She was brought to her home where she became anemic and vomited frequently. She was bruised over the regions of the liver and the spleen. The next day as the child had repeated nosebleeds, nose specialist was called who treated the hemorrhage with caustery. For few days she was better but was not able to leave the bed. She became increasingly pale and weak but had no fever. Eight days before admission the nosebleed recurred. She vomited light blood both then and on 21. Later she could not lie on the right side.

**Examination**—The patient was an extremely pale and emaciated looking 11 year-old girl. There was some tenderness over the liver and the spleen. The liver could be palpated 4 cm. below the costal arch.

The child lay steadily on the left side and did not exert it on over on her back. The urine contained many red blood corpuscles. Hemoglobin was 77 per cent. It was supposed that she had a central liver rupture, possibly portal thrombosis. The child was treated for two months before she died.

Now and then the temperature rose to 38.5 C. for few days. During these days the pain in the liver region became worse and she vomited frequently. During the three first weeks the stools were tarry from blood, then diarrhea. After ten weeks the hematemesis disappeared. The anemia could not be financed and the hemoglobin sank to 19 per cent. The liver region remained tender but the lower border of the liver was palpated at different levels. For short time the child was in better condition but then she again had severe pain in the liver region. From that time on she lost rapidly weight and had unbearable pain until she died.

**Autopsy**—At autopsy the following was found. In the right lobe of the liver there was a cavity the size of child's head, covered by the right diaphragm. The liver capsule was intact. The cavity contained blood clots and brownish red fluid.

There were multiple subpleural and subpericardial ecchymoses. There also were numerous small hemorrhages in the mucosa of the small intestine and solitary ones in both kidney pelves.

Microscopic sections of the liver showed both old and recent necrotic areas. In the center of the latter there were signs of fresh hemorrhages.

**Wulsten comments**—A long-standing hematuria and blood in the stools for weeks with tarry stools as late as five weeks after the injury have never been described. These signs can perhaps be of help in the diagnosis.

**Comment**—The liver rupture in this case gave rise to a large cavity. The type of pain was similar to that in Case 4 and indicates that the lesion had a subcapsular location from the start. Judging from the outcome of Cases 5, 7 and 8 where the cavities were of similar size the child could perhaps have been saved by an early operation with drainage of the cavity.

The striking features in this case were the marked anemia and the protracted hemorrhage. At autopsy there were found multiple subpleural and subpericardial ecchymoses, numerous small hemorrhages in the mucosa of the small

intestine and solitary ones in both kidney pelvis. These were supposed to be of toxic origin. Another possibility is that they were caused by the sudden increase in the venous pressure when the thorax was compressed.

The blood in the vomit and in the stools could have originated from these hemorrhages in the mucosa. Considering the large amounts of blood that were lost and with the experience gained from Cases 2 and 3 it seems more likely that the blood came from the liver lesion. The changes in volume of the liver that are described could have been due to evacuation of blood through the ducts alternating with hemorrhage from the wall of the cavity.

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**Case 7**—A 19 year old laborer was admitted after having been run over by an automobile while bicycling. He was in a state of severe shock on admission. He had fracture of the left forearm and also an extraperitoneal rupture of the bladder which was operated upon.

After an improvement of a few days he suddenly had an intense pain below the right costal margin, radiating to the right shoulder. No explanation was found in the chest for this pain. The abdomen was soft and not tender. The piercing pains continued for a few days but then there appeared marked tenderness to pressure over the liver with reactionary abdominal rigidity.

Five weeks after the accident his condition became worse. He became icteric and had violent attacks of vomiting. The liver region remained just as tender but it was also noted that the liver was markedly enlarged.

*Operation*—Operation was then carried out. There was no blood in the abdominal cavity and no peritonitis. The liver was enlarged to twice the normal size and the consistency distended like a balloon (the biliary ducts are not described). Upon puncture of the liver a cavity was found at least more than 1 cm. thick in wall of parenchyma. From this 3 liters of fluid consisting of bile and blood, were emptied, after which the liver collapsed. The cavity was dried and in the beginning there was abundant secretion but six weeks later the wound was healed. The patient recovered.

Holm concluded that this was a case of central rupture of the liver, noteworthy because of the unusual amount of bile mixed with blood that was found in the cavity.

*Comment*—In this case there was undoubtedly a central rupture of the liver with an accumulation of bile and blood. The severe pains below the right costal margin radiating to the right shoulder had a definite character of biliary colic. They can hardly be explained by the swelling of the liver with distention of the capsule as the abdomen then was entirely soft and not tender. The tenderness did not appear until after several days, and the sign of hepatic enlargement appeared still later. The course in this case is best explained by the presence of blood clot in the biliary tract.

The following case was reported by Ben Iberg from the Lund Hospital in 1906.

**Case 8**—A boy aged 14 years was knocked down by a bus and was hospitalized on the following day. On admission right leg fracture of the olecranon was established and operated upon. There was some tenderness in the right side of the abdomen from the navel up into the epigastrium. There was fracture of the pelvis and

lesion of the right kidney (tenderness + pressure over the kidney and hematuria). These lesions healed without complications. The patient had slight increase in temperature. The tenderness in the abdomen declined and the hematuria disappeared. Few days after admission the patient had attacks of sudden pain, radiating from the epigastrium out to the left shoulder. The attacks lasted five to ten minutes, came on several times a day and were frequently so severe that the patient groined aloud. Between the attacks of pain the patient had no discomfort. Gradually the attacks occurred more seldom, but on the other hand the patient began to complain of continuous sensation of tenderness in the epigastrium. There was a concomitant increasing enlargement of the liver, the liver finally reaching the level of the umbilicus. Urine and feces were normal in color. X-rays were observed.

*Operation*—Laparotomy as performed one month after the accident. The greatly enlarged liver showed no external lesions but fluctuated markedly. After incision of the abdominal cavity the liver was incised and at the depth of 1 cm. cavity was found which was seen to contain 2 liters of bile. Drainage was carried out. The first days following operation the feces were entirely chole and an abundant amount of bile flowed out into the bandages. The bile flow soon ceased, the feces regained normal color and about six weeks postoperatively the patient was discharged, entirely cured.

I have learned from the hospital that the feces were not examined for blood until the time of the operation, that is, after the attacks of pain had ceased. The tests were then negative.

Brandberg discussed the intense pain in his and Holm's patients (Cases 8 and 7). The difference in the irradiation—in Holm's case through the right shoulder in his own through the left shoulder—he explained by the fact that in the first case the rupture was mainly in the right part of the liver in the second case in the left part. Brandberg found that those two cases are arguments against the general applicability of the rule that central ruptures of the liver do not cause pain.

He concluded that the distention of the liver is more important as cause of pain than the localization of the lesion.

*Comment*—Brandberg's case was very similar to Holm's and was also a case of true central liver rupture. The attacks of violent pain of short duration with intervals free from discomfort can best be explained by the passage of blood clots. The only atypical trait is the irradiation through the left shoulder.

It is difficult to understand how these attacks could have come from a distention of the capsule because the patient was free from symptoms between the attacks. The liver did not become enlarged until later. Then there also was a continuous sensation of tenderness in the epigastrium such as one would expect from a distended capsule.

This case history seems to demonstrate clearly the difference in pain occasioned by the passage of clots as compared to the pain from a distended capsule both occurring successively in the same case.

Castrén of The Hospital of the Red Cross of Finland described the following case in 1916.

*CASE 9*—A 14-year-old boy was knocked down by an automobile and was pushed 10 meters by one of the front wheels. He could walk alone about 500 meters but after five hours he could not move and could not even lie on his back. His comrades brought him to

the hospital. He was then in a state of shock but was perfectly conscious. He had bruises on the right elbow on the right side of the pectoral, and on the lower part of the costal margin. There was tenderness in the right side of the back corresponding to the lower ribs. There was microscopic hematuria which disappeared on the third day. The hemoglobin was 49 per cent. On the fourth day he was discharged with the diagnosis of abdominal contusion (rupture of the right kidney?).

He stayed in bed at home and everything was well until the eighth day when he felt pain in the right lower part of the chest increasing with the respiration. On the tenth day he had such violent pains in the epigastrium that he doubled up and was short of breath. At the same time there was increasing tenderness in the back. He was then brought to the hospital again.

At examination he looked ill as pale and the hands and feet were cold. There was tenderness in the abdomen, especially under the right costal arch. Hemoglobin was 60 per cent. The urine contained albumin, some hyaline and granulated cylinders and leucine crystals. At x-ray examination the right diaphragm showed decreased elevation.

The pains decreased at first but on the sixteenth day he had violent attack of severe pain radiating through the right shoulder. The liver of firm consistency could be felt in the mamillary line two fingerbreadth below the costal arch. At that point there was extreme tenderness. Hemoglobin was 55 per cent, temperature 38.1 C.

Ten days later the pains had disappeared, there had been no fever for one week. The liver was unchanged. One month later he was back at work without symptoms. The diagnosis was central rupture of the liver.

Castroń was fairly certain that there was a central rupture of the liver in this case. Besides the story and clinical signs there was also biliary pigment in the urine indicating liver damage. The finding in the urine of albumin and cylinders made him believe that there also was a hepatorenal syndrome. He did not discuss the pain in this case. I wrote to the hospital and found that the stools were not examined for blood.

*Comment*—In this case the diagnosis was not verified. A liver injury seems most likely but it is difficult to say whether there was a central or a subcapsular rupture. The attacks of pain may have been due to increasing collection of blood under the capsule. The simultaneous tenderness in the liver region supports this explanation. On the other hand, the marked anemia indicates a large loss of blood than could well be occasioned by a moderate hematoma in the liver. The repeated attacks of violent pain of short duration may well have been caused by blood clots in the biliary duct.

In this case there is thus a possibility that there was a hemobilia with biliary colic caused by a subcapsular liver lesion. The probability seems somewhat less than in the two preceding cases.

#### DISCUSSION

Nine cases have been collected in which trauma to the liver region has resulted in a hemorrhage in the biliary tract. A subcapsular lesion was proved by autopsy or operation in six of the cases (Cases 3 to 8). In the remaining three cases such a lesion seemed highly probable for the reasons mentioned. The presence of blood in the biliary tract was proved in three cases (Cases 1 to 3); it was highly probable in five (Cases 4 to 8) and at least possible in one (Case 9).



lesion of the right kidney (tenderness to pressure over the kidney and hematuria). These lesions healed without complications. The patient had slight increase in temperature. The tenderness in the abdomen declined and the hematuria disappeared. Some 4 days after admission the patient had attacks of sudden pain, radiating from the epigastrium out to the left shoulder. The attacks lasted five to ten minutes, came on several times a day and were frequently so severe that the patient groaned aloud. Between the attacks of pain the patient had no discomfort. Gradually the attacks occurred more seldom, but on the third day the patient began to complain of constant sensation of tension in the epigastrium. There was a concomitant increasing enlargement of the liver, the liver finally reaching the level of the umbilicus. Urine and feces were normal in color. No icterus was observed.

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collects and forms a cavity. This is clearly demonstrated in Cases 7 and 8 (probably also in Case 4). When the attacks of biliary colic subside the liver becomes enlarged and a continuous sensation of tension in the epigastrium results. Large cavities containing a mixture of bile and blood may be found upon operation or autopsy. In other cases a clot in a central duct may loosen and get pushed out with a large gush of blood (Cases 9, 8 and 4).

The symptoms of hemobilia have often been misinterpreted (Cases 1, 2, 4, 7 and 8). When this symptom is understood and the signs of it are looked for a clearer conception and a more certain diagnosis of many cases of subcapsular liver lesions will be obtained.

## SUMMARY

1. Nine cases (one reported herein and eight collected from the literature) of subcapsular liver injuries presenting a certain or probable hemorrhage to the biliary tract have been studied. This symptom has been named hemobilia.

2. Hemobilia may cause (a) hematemesis and melena, (b) biliary colic, (c) biliary obstruction or (d) gall bladder distention.

3. Hemobilia should be looked for in all cases of liver injuries with vague symptoms. It might be a frequent symptom of value in the diagnosis and understanding of these cases.

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Considering that these nine cases have been taken from a collection of twenty cases and that blood in small quantities in the bile ducts is likely to be overlooked it seems justified to conclude that hemorrhage into the biliary tract or hemobilia is a frequent symptom in subcapsular liver lesions. (There have been cases described of central liver ruptures where there was no escape of bile, indicating that no bile radicals were injured [Robertson<sup>27</sup>]. One could not expect a hemobilia of importance in such a case.)

The course and the signs of hemobilia can be studied in the nine cases described.

In minor liver injuries, which although apparently not infrequent are seldom recognized because of their vague symptoms, a slight hemobilia could be expected to give an occult melena. In Case 1 where a hemobilia was verified, the test for occult blood in the stools was positive. It is recommended that this test be made in all cases where a liver injury is suspected, but where the symptoms are uncertain.

A more pronounced hemobilia causes hematemesis (Cases 3 and 6) or melena (Cases 1 to 6). A secondary anemia may result (Cases 1, 3, 5, and 9) sometimes severe (Cases 4 and 6).

It may be difficult to decide whether the hemorrhage originates in the digestive tract or in the liver (Case 6). The sudden increase in the venous pressure caused by the compression of the thorax which usually occurs in these cases may give rise to multiple small hemorrhages and to epistaxis (Cases 4 and 6). A protracted hemorrhage lasting for weeks or months is most likely to be due to hemobilia. The bile mixed with the blood delays clotting and the clots in the liver parenchyma have little power of contraction.

If the blood clots in the biliary tract new events occur.

The passage of the clots causes pain which has the character of biliary colic (Cases 1 to 4 and 7 to 9). The passage of a clot has been proved in a few cases where it was found in the vomit (Case 3) or in the stools (Case 1). When the clot has passed the attack may stop definitely (Case 3) or until new clots are formed (Case 1). It seems that clots consisting of a mixture of blood and bile become rather tough in consistency (Cases 1 and 3).

When the clots do not pass but obstruct the ducts, jaundice naturally results as in Cases 2 and 3. It may subside when the clot passes.

I have not found any case where a permanent obstruction of the common duct was with certainty due to a coagulum. (Luncke<sup>28</sup> described a 6-year-old boy who was operated upon for a total obstruction and where there were signs of a central liver lesion. Although it is possible that the obstruction was caused by a coagulum, it seems equally possible that a constriction of the common duct was caused by a concomitant injury to the surrounding tissues.)

If the blood clots in the gall bladder it acts in the same way as a gallstone (Cases 1, 2, and 3) producing characteristic pain and tenderness. A distended gall bladder may be palpated (Cases 1 and 3). It is even probable that the clot will become impacted and cause distention gangrene (Case 1).

As long as the blood flows freely from the rupture it is probable that a large cavity will be formed, but when the biliary ducts are closed off fluid

# In Memoriam

ALBERT O SINGLETON

1889 1947

ALBERT O SINGLETON, professor of surgery at the University of Texas School of Medicine, died at his home in Galveston on June 12, 1947, of coronary artery disease. He was widely known as an outstanding surgeon and medical educator and was, in addition, greatly beloved by many friends both within and outside the profession.

He belonged to a small group of surgeons, now rapidly disappearing in an age of increasing specialization, who could perform almost any type of operation well. He was also recognized as a leader in the adoption of new surgical techniques and procedures. He was an early advocate of upper intestinal decompression as a routine postoperative measure and he realized the importance of maintaining proper fluid and electrolytic balance in his patients at a time when administration of parenteral fluids was considered a radical procedure. He was the first man in the state of Texas to perform a total gastrectomy, a pneumonectomy, and closure of a tracheo-esophageal fistula. Because of his vast amount of experience in many fields of surgery, he could write and talk authoritatively on a wide variety of subjects. His best known papers dealt with the problem of wound disruption, the use of anatomic incisions, cancer surgery of the large bowel, diseases of the lymphatics, splenectomy, and the newer aspects of thoracic surgery. He continually stressed the importance of fundamental anatomy, physiology, and pathology in the treatment of the patient, and felt that all progress in surgery must rest upon advances in these basic sciences. In addition to his medical writing, he was particularly interested in the history of medicine in Texas and chose as his presidential address for the Southern Surgical Association in 1939 an account of "The Surgeon in the Romantic History of Texas."

As a clinical teacher of surgery in the wards and as an operating room demonstrator, Dr. Singleton was at his best. He was a master technician, bold and decisive as an operator but ever cautious in his handling of the tissues. His remarks were punctuated by wit and emphasized by brevity.

Dr. Singleton received his surgical training under Dr. James E. Thompson, having been granted his medical degree from the Medical Branch of The University of Texas in 1910. He was associated with the institution for thirty years and was appointed professor of surgery and chief surgeon of the John Sealy Hospital upon Dr. Thompson's death in 1937. He worked constantly for the betterment of the hospital and medical school and was instrumental in bringing to fulfillment a program of expansion of the physical plant as well as setting up the first postgraduate program in Texas for specialty training. Under his leadership, the department of Orthopedics, Genitourinary Surgery, Thoracic Surgery, and Plastic and Maxillo-facial Surgery were set up and provisions were made for animal research. Because of his untiring efforts, the Medical School was able to establish a number of years ago, an Anesthesia Department of the first class.



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A member of the Founder's Group of the American Board of Surgery Dr Singleton served on the Board of Governors of the American College of Surgeons from 1937 to 1940. He was also vice-president of the latter organization in 1939-1940 and had been president of the Southern Surgical Association, president of the Texas Surgical Society and vice president of the American Surgical Association. He was also a member of the editorial staff of *Surgery*. He belonged in addition to the American Association of Thoracic Surgery, the International Surgical Association, the American Association for the Surgery of Trauma, the American Cancer Society, Kappa Sigma, Phi Alpha Sigma, and Alpha Omega Alpha. He was an active participant in organizational meetings, enjoying keenly the stimulation of association with surgical colleagues and contributing greatly himself to scientific discussion of surgical problems.



Albert O. Singleton

Dr Singleton was genuinely devoted to his family and home. He is survived by his wife, the former Miss Will Dean Bivens, and by two sons, Dr Albert O. Singleton, Jr., and Dr Edward B. Singleton.

Dr Singleton stood always for the highest personal and professional ideal. His name must be added to the list of illustrious surgeons in the Romantic Story of Texas.

—T. G. Blocker, Jr.

# Book Reviews

**Aseptic Treatment of Wounds.** Carl Walter M.D. New York, 1949. The Macmillan Co.

This work is typical of surgeons and nurses concerned with this important problem. The book represents a complete study of every phase of the subject. Most modern surgeons and nurses in charge of operating theaters have received their training from those who provided them. The technical preparation of materials for use in the operating rooms and the principles of asepsis have been handed down from generation to generation without questioning the validity of the procedures. The surgeons and nurses at the beginning of the century were more intimately concerned with methods because they were the practical testers of the laboratory theories. They scrutinized the techniques with care and with understanding of the underlying purpose of each step. As tested techniques developed they were accepted or discarded. By the time of World War I the majority of these surgical preparations and procedures had been gradually fixed for general use. The only minor variants remain.

Walter's book traces the historical development of the aseptic principle. The step-by-step progression from the first recognition of the infectious nature of sepsis to the complete triumph of aseptic sterilization is expounded with accuracy and complete documentation. Formative little pages of the important first discoveries lend interest to the manuscript.

The chemical destruction of bacteria is carefully considered. The estimation of the value of given chemicals against the various types of microorganisms is presented with the proper cautions necessary to really define their worth. The common antiseptic chemicals such as alcohols, chlorinated compounds, iodine formaldehyde, the mercurials, the phenols and the quaternary ammonium compounds are all compared as to their value against bacteria in varied situations. The chemical disinfection of instruments is treated from a practical every-day standpoint. Technical detail of total contamination of sterilized instruments are all illustrated. This makes the book an ideal reference book for training younger members of the medical and nursing professions. The care necessary to maintain the cutting edges of instruments is well considered. Sterilization of utensil ampules, rubber goods, instruments with optical lenses, plastics, brushes, suture materials etc., is made clear and possible and rules in their handling pointed out.

The use of physical agents to destroy bacteria is reviewed. The effect of light, pressure, radiation, dry and moist heat are given consideration. Sanitization by boiling water is noted as important. The construction of sterilizers so that there is proper venting with mechanisms to prevent backflow contamination is shown by numerous drawings. A step-by-step explanation of safeguard the sterility of the prepared materials.

Sterilization by steam has many pitfalls but these are enumerated. The types of steam sterilizers are compared. Their advantages and disadvantages are set forth. Mistake in using compressed steam is pointed out. The control of steam sterilization and methods for testing are carefully tabulated.

Sterilization of dressings and dry goods is illustrated by packaging for a plaster cast. The complete procedure is presented from the preparation of the wrapper, the assembling of supplies, the wrapping and taping of the cast, even to the type of knots—simply illustrated step by step. The steps in folding laparotomy sheets, gowns, the making of sponges, pad packs, etc. are listed fully shown. An operating room or nursing school should be without this book because of the detailed uniform type of procedure.

The care of instruments then sterilizing is the care of hollow needles and glass syringes, dry and wet techniques for rubber gloves and every phase of preparation of material for aseptic use are explained briefly so that nothing is left to chance.

Complete details of every conceivable type of operative procedure are given from the wrapping of the team, the preparation of the nurse, tables, the disposal of the waste, the dressing of the gown and gloves, the disinfection of the operative field, the draping of the patient, the position of the patient, and the actual operating room technique in the



aseptic handling of external eyes to the placing of the sutures. These measures are given line drawing treatment omitting no detail which may help to clarify measures to diminish the airborne entrance to the dressed side such head eyes as washing, scrubbing, and ultraviolet light installations.

The last chapters of the book are concerned with the decontamination and restoration of instruments and wounds after septic cases. Measures to determine that contamination will not be spread are again well shown by illustration. The preparation of parietal fluids so that these are convenient and easy to use has long been one of Walter's pet projects. His director of central preparation room or Red Cross blood procurement center can afford to pick up the wealth of information given in these chapters on solutions and blood and plasma facilities. The control measures necessary to prevent the spread of communicable diseases from one part of the hospital to another are also well covered. The final chapter has to do with the proper maintenance of sterilizing equipment. It is replete with many useful suggestions gained by intimate firsthand observations under actual running conditions.

### Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

**OSTEOTOMY OF THE LONG BONES.** By Henry Mink, M.D. Consulting Orthopedist, Massachusetts Hospital. Cloth. Price \$6.75. Ed. 3. Pp. 326, with 500 illustrations. Springfield, Ill. 1947 Charles C Thomas, Publisher.

**A SHORT HANDBOOK OF PRACTICAL ANAESTHETICS.** By Basil Perry Price, Surgeon Commander U.D.R.M.U.R. Cloth. Price \$3. Ed. 1. Pp. 190, with 40 illustrations. Bristol, 1946, John Wright & Sons, Ltd.

**SURGERY OF THE AMBULATORY PATIENT.** By L. Aracer Ferguson, A.B. M.D. F.A.C.S. Cloth. Price \$10. Ed. 1. Pp. 901 with 645 illustrations. Philadelphia, 1947 J. B. Lippincott Company.

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# SURGERY

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## Original Communications

### ETIOLOGY OF ACUTE PANCREATITIS

#### AN EXPERIMENTAL STUDY

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ACUTE pancreatitis is characterized by the dramatic onset of abdominal pain, nausea, vomiting, and collapse even to the state of shock. In rare cases, abdominal trauma, rupture of an aneurysm, or infections are responsible, but in the large majority the etiology is not definitely established.

The pathology of acute pancreatitis varies considerably. Although some have regarded the degrees of involvement as different diseases entitled, it is probable that they are stages of the same process. In the cases that come to autopsy the inflammatory process is usually patchy. Some part of the gland shows destruction of the lobules, others show necrosis of a few acini around the periphery of the lobules, and still others show normal lobules with inflammatory cells in the interlobular septa. Fat necrosis is irregular in its distribution. When the walls of blood vessels are involved, one finds hemorrhagic areas intermingled with the areas of fat necrosis and parenchymal destruction. At a later stage when the pathology has had time to develop one finds degrees of inflammation ranging from a few leucocytes to abscess formation.

In the American literature Fitz, 1879 is generally credited with first describing the pathology of acute pancreatitis, whereas Robert gave a detailed account of a case in 1889. In 1901 Opler performed an autopsy on a patient who had succumbed to acute pancreatitis, and found a stone impacted in the ampulla of Vater. From this evidence he postulated that acute pancreatitis was caused by an impaction of a stone at the ampulla of Vater thus leading to a retrograde flow of bile along the pancreatic tree. This observation has led to a great deal of investigative work which aimed to prove or disprove the common channel theory. The evidence has been summarized and discussed by Ravdin and Johnston. We will review only a few of the salient points in this argument.

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spaces. In confirmation of this criticism we have the observation by Mann and Giordano that pancreatitis cannot be produced by retrograde injection of bile if the pressure exerted is within physiologic limits.

The experiments in which a common channel was formed between the bile and pancreatic ducts are open to a further criticism for they involve obstruction of the pancreatic duct. What would happen under the identical experimental conditions if only the pancreatic ducts were tied has not been studied as a control. Furthermore it is not reported in detail whether animals used for the experiment were fed or starved—a most important consideration in dealing with the pancreas.

A theory regarding the etiology of acute pancreatitis which held the attention of clinicians some years ago was the spread of infection from the gall bladder through the retrograde flow of lymph. A review of the evidence on this subject seems scarcely necessary for this concept does not bear careful scrutiny. Radwin and Johnston have summarized the evidence against its validity.

One of the considerations which has made the common channel theory and the resultant flow of bile into the pancreas tree so attractive has been the activation of trypsin produced by bile. Some explanation had to be offered for the activation of trypsinogen into trypsin in order to account for the autodigestion of the pancreas in acute pancreatitis. That bile is not essential for this activation is apparent when one considers the great number of agents that will activate trypsinogen. According to Bakken<sup>12</sup> Helix bile, human saliva, trypsin extract, bacteria and other substances will activate trypsinogen. If the pancreatitis just is expressed into the pancreatic tissues trypsinogen will therefore be activated immediately by the alkaline ions. Lipase and amylase are secreted in active form and enable the secretions when they reach the tissue spaces. Dragstedt, Himmelfarb and Ellis<sup>13</sup> argued against the capability of pancreatic juice to digest pancreatic tissue. They sutured the tail of the pancreas into the duodenal wall so that the tail of the duodenum became it could act on it. Since no digestion occurred they concluded that pancreatic juice is harmless without the action of another factor. In acute pancreatitis the pancreatic secretion is extruded into the tissue of the gland presumably under pressure of it must burst the finer blood vessels and reach the intercellular spaces. This is a far different set of circumstances from mere passive contact of the juice with the surface of the gland. The photomicrographs presented by Dragstedt and associates<sup>13</sup> show a heavy layer of fibrous tissue on the surface of the pancreas indicating that the duodenal content have no direct contact with the pancreatic area.

In the experiment of Polak<sup>14</sup> acute pancreatitis was produced by retrograde injection of small amount of pure trypsin into the pancreatic duct. The same result were obtained by Radwin and Duff.<sup>15</sup> Both investigators failed to produce pancreatitis with an equal amount of heated or inactivated trypsin. Once the pancreatic juice reaches the tissue spaces it begins to produce necrosis and inflammation. The main point is therefore to determine how the pancreatic juice reaches the tissues.

From 200 consecutive autopsies, Mann and Giordano<sup>10</sup> concluded that a common channel between the two ducts could be produced by a stone at the ampulla in only 3.5 per cent of cases. Rlenhoff and Pickrel<sup>11</sup> studied the bile and pancreatic duct systems in 100 autopsies and concluded that a common channel could be produced through blockage of the ampulla in 17 per cent of the patients. Mann and Giordano paid particular attention to the distribution of the circular muscle fibers constituting the sphincter of Oddi. They found on serial section that this muscle group extends along both the pancreatic and bile ducts—a finding that was confirmed by Borden.<sup>12</sup> Should contraction of the muscles occur so as to occlude the ampulla, the two ducts would be shut off from each other and a common channel would be impossible. Cameron and Noble<sup>13</sup> found that in 66 per cent of 100 routine autopsy specimens, reabsorption of bile along the pancreatic ducts was possible. This work, however, fails to consider the factor of muscle contraction. Upon the basis of anatomical evidence alone, one must conclude that in the majority of cases, a retrograde flow of bile does not cause a bile pancreatitis.

Cases of acute pancreatitis have been reported in which the common channel theory was not an acceptable explanation. Outstanding in this group are the ones which describe acute pancreatitis in the region of the gland which is drained entirely by the duct of Santorini.<sup>14</sup> This duct has a separate opening in the duodenum quite apart from the bile duct. A retrograde flow of bile will not explain the disease in these cases. In another group of cases where death followed acute pancreatitis, the duct of Wirsung opened separately from the common duct into the duodenum.<sup>15</sup> Mann and Giordano<sup>10</sup> studied eleven cases of acute pancreatitis at autopsy and in none of them was a common channel possible from an obstruction at the ampulla of Vater.

More recently radiographic studies have been made in patients with a T tube in the common duct. Rayli and Johnston reviewed the evidence that obtained and found that in 90 per cent of cases there is free flow of bile into the pancreatic tree. Such cases do not develop acute pancreatitis even though bile enters the pancreatic duct. It is quite reasonable to assume that in the patient where a common channel is possible between the two ducts there is free flow of bile into the pancreatic duct and vice versa depending upon the relative pressures in the two systems.

Finally, there is the criticism of the animal experiment which produced acute pancreatitis by a retrograde injection of bile along the pancreatic duct. Rich and Duff<sup>16</sup> showed that the pressures used for such retrograde injection were unphysiologic. They used a piece of India ink for retrograde injection and noted that even such small amounts ruptured the ducts and led to an extrusion of the carbon particles into pancreatic tissue. In experiment with retrograde injection of bile into the pancreatic duct as much as 5 to 10 c.c. was used.<sup>17</sup> Archibald used pressures up to 100 mm. Hg, whereas physiological pressures do not exceed 3 mm. of bile. We must conclude that in all of such experiments, rupture of the pancreatic duct—complicating factor with it results in injury to the gland and release of pancreatic juice into the intercellula

spaces. In confirmation of this criterion we have the observation by Mann and Giordano that pancreatitis cannot be produced by retrograde injection of bile if the pressure exerted is within physiologic limits.

The experiments in which a common channel was formed between the bile and pancreatic duct are open to a further criticism for they involve obstruction of the pancreatic duct. What would happen under the identical experimental conditions if only the pancreatic ducts were tied has not been studied as a control. Furthermore, it is not reported in detail whether animals used for the experiments were fed or starved—a most important consideration in dealing with the pancreas.

A theory regarding the etiology of acute pancreatitis which held the attention of clinicians some years ago was the spread of infection from the gall bladder through the retrograde flow of lymph. A review of the evidence on this subject seems scarcely necessary if this concept does not bear careful scrutiny. Rardin and Johnston have summarized the evidence against its validity.

One of the considerations which have made the common channel theory and the resultant flow of bile into the pancreatic tree so attractive has been the activation of trypsin produced by bile. Some explanation had to be offered for the activation of trypsinogen into trypsin in order to account for the auto-digestion of the pancreas in acute pancreatitis. That bile is not essential for this activation is apparent when one considers the great number of agents that will activate trypsinogen. According to Babkin<sup>14</sup> HCl, bile salts, albumen salts, tissue extracts, bacteria and other substances will activate trypsinogen. If the pancreatic juice is expressed into the pancreatic tissues, trypsinogen will therefore be activated immediately by the bile salts. Lipase and amylase are secreted in active form and can, therefore, act at once when they reach the tissue spaces. Dragstedt and Hammond, and Ellis<sup>15</sup> argued against the capability of pancreatic juice to digest pancreatic tissue. They cutured the tail of the pancreas into the duodenal wall so that the active duodenal contents could act on it. Since no digestion occurred they concluded that pancreatic juice is harmless with out the action of another factor. In acute pancreatitis the pancreatic secretion is extruded into the tissue of the gland, presumably under pressure for it must burst the fiber in its walls to reach the interlobular spaces. This is a far different set of circumstances from a mere passive contact of the juice with the surface of the gland. The photomicrographs presented by Dragstedt and associates<sup>16</sup> show the presence of fibrous tissue on the surface of the pancreas, indicating that the duodenal contents have no direct contact with the pancreatic tissue.

In the experiment of Polya<sup>17</sup> acute pancreatitis was produced by retrograde injection of small amount of pure trypsin into the pancreatic duct. The same results were obtained by Rich and Duff. Both investigators failed to produce pancreatitis with an equal amount of heated or inactivated trypsin. Once the pancreatic juice reaches the tissue spaces it begins to produce necrosis and inflammation. The main point is, therefore, to determine how the pancreatic juice reaches the tissues.



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One of the considerations which has made the common channel theory and the resultant flow of bile into the pancreatic tree an attractive has been the activation of trypsin produced by bile. Some explanation had to be offered for the activation of trypsinogen into trypsin in order to account for the autodigestion of the pancreas in acute pancreatitis. That bile is not essential for this activation is apparent when one considers the great number of agents that will activate trypsinogen. According to Bakum<sup>22</sup> HCl, bil, calcium salts, trau extract, lactia and other substances will activate trypsinogen. If the pancreatic juice is expressed into the pancreas trypsinogen will therefore be activated immediately by the alkalium ion. Lipase and amylase are secreted in active form and can, therefore, act at once when they reach the tissue spaces. Digestit, Haymon<sup>1</sup> and Ellis<sup>23</sup> argued against the capability of pancreatic juice digesting pancreatic tissue. They sutured the tail of the pancreas into the duodenal wall so that the active duodenal content could act on it. Since no digestion occurred they concluded that pancreatic juice is harmless without the action of anther factor. In acute pancreatitis the pancreatic secretion is extruded into the tail of the gland, presumably under pressure for it must burst the finer duct wall to reach the intercellular spaces. This is a far different set of circumstances from a mere passive contact of the juice with the surface of the gland. The photomicrographs presented by Digestit and associates<sup>24</sup> show a heavy layer of fibrous tissue on the surface of the pancreas, indicating that the duodenal content has no direct contact with the pancreatic acini.

In the experiment of Polva<sup>25</sup> acute pancreatitis was produced by retrograde injection of small amount of pure trypsin into the pancreatic duct. The same result were obtained by Rich and Duff.<sup>26</sup> Both in this it is failed to produce pancreatitis with an equal amount of heated or inactivated trypsin. Once the pancreatic juice reaches the tissue spaces it begins to produce necrosis and inflammation. The main point is, therefore, to determine how the pancreatic juice reaches the tissues.

We find in the literature a number of observations pointing to the etiology of acute pancreatitis. Coffey produced acute pancreatic inflammation and fat necrosis in dogs by ligating the main pancreatic duct and administering pilocarpine. His experiments are open to the criticism that he avulsed the lesser pancreatic duct thereby allowing pancreatic juice free access to the peritoneal cavity. Wangensteen and associates also produced fat necrosis and inflammation of the pancreas in cats by ligating the major duct and giving pilocarpine. One of us (R.L.) unpublished observations noted in some experiments performed with Florey that there was an acute inflammatory reaction in the pancreas of cat after prolonged stimulation of the vagus nerves with the pancreatic ducts ligated. Hess<sup>11</sup> found that ligation of the pancreatic ducts in dogs at the height of digestion produced acute pancreatitis and fat necrosis. This did not occur if the ducts were ligated in starved animals. Wangensteen and his co-workers were able to produce acute pancreatitis by ligating the ampulla of Vater in cats and administering fatty meals. They did not perform the same experiment with simple ligation of the pancreatic duct as a control.

Wangensteen and associates, after an exhaustive study of experimental pancreatitis in cats, concluded that this disease represents not one but perhaps several factors working in combination. These experiments all have two factors in common—(1) obstruction to the pancreatic ducts in the presence of a (2) secreting or stimulated gland. We believe that these two factors are responsible for most cases of acute pancreatitis. Rich and Duff<sup>12</sup> came to a similar conclusion from their study of human autopsy material. The present study is experimental confirmation of the evidence which these authors collected from human material. It seems unfortunate that Rich and Duff should have been quoted so widely in the literature as explaining acute pancreatitis by obstruction due to proliferation of ductal epithelium. A careful reading of their paper shows that their most important idea is blockage of a secreting gland, and that ductal hyperplasia is only one form of such blockage.

#### EXPERIMENTAL

It was the object of these experiments first to obstruct the pancreatic duct and then to stimulate the gland by various means. Feeding is the natural stimulant of the pancreas. An parasympathomimetic agent will evoke secretion. Vagal stimulation, acetylcholine, pilocarpine and eserine are such agents. There is also a hormonal stimulation peculiar to the pancreas—secretin. This agent is elaborated in the duodenum by the action of acid on the duodenal mucosa. Secretin elicits a secretion poor in amylase and quite watery whereas vagal stimulation elicits a thick secretion quite rich in enzymes. It seems likely that the enzymes are formed in the pancreas during the early phase of digestion through vagal stimulation and then are washed out by the flow of secretin which is formed and absorbed in the stomach content reach the duodenum. The simplest way to be certain of a secretion rich in enzymes is to feed the animal.

Man experiments were performed in which the animals were fed two hours before ligation of the ducts. The animals were then given secretin, pilocarpine, or acetylcholine and eserine. It was found that the degree of pancreatitis was not increased over that obtained by feeding and tying the ducts without further stimulation. In subsequent experiments starved animals were used when these agents were administered.

Medium-sized cats of both sexes were used. Under ether anesthesia a midline upper abdominal incision was made using sterile precautions. By very gentle dissection the greater and lesser pancreatic ducts were located. Ligation of the greater duct is fairly simple. It enters the duodenum at the side of the common bile duct and is usually 1 to 2 mm in diameter. The lesser duct may be rather elusive, as it is covered by glandular substance and may be only the size of a fine thread. It is best approached from the side opposite to the entrance of the large duct. At first we were unable to locate this duct in many animals and our results were quite variable. After perfecting the operative technique we were able to find the lesser duct in all of the cat. We include in our experimental reports only those animals where both greater and lesser ducts were found.

Two sets of experiments were performed with each method of stimulating the pancreas. In one group the ducts were located but not tied; in the other a silk ligature was placed around both ducts. In this way the element of surgical trauma was eliminated as a source of pancreatic inflammation.

Secretin was given intravenously using a total of 10 to 20 units in divided doses during the experimental period. Pilocarpine was administered subcutaneously in 0.6 mg. doses, repeated twice a day throughout the experiment. One milligram of acetyl-beta-methylcholine was combined with 0.6 to 0.4 mg. eserine for each dose. This also was repeated twice a day. When the animals were fed they were given chopped liver and milk. In a separate group of experiment the ducts were tied and 100 cc. of 90 per cent cream was administered by stomach tube immediately after laparotomy. This was repeated under light ether narcosis twice a day until the animal was sacrificed.

The cats were observed for a varying period. The best time for sacrifice seemed to be twenty-four hours or forty-eight hours, and most of them were killed by ether inhalation at the end of this time. Because the operative trauma might give an inflammatory reaction sections of the gland were taken through the tail of the pancreas at a considerable distance from the ligatures. The tissues were fixed in Zenker's solution and stained with phloxine-methylene blue.

In all animals that had a simple laparotomy with exposure of the ducts, but without ligation, there was no fat necrosis seen. Normal pancreatic was found on microscopic section (Fig. 1). The same results were obtained when the ducts were tied in starved animals and no stimulant administered (Fig. 2). Hepatic results were obtained when the animals were fed, or given pilocarpine, secretin, or acetylcholine and phoslogamine with the duct intact. When the

The preparations of secretin were used, one secretin Astra and the other secretin furnished by the W. G. Corporation. Both preparations seemed to have the same amount of activity.

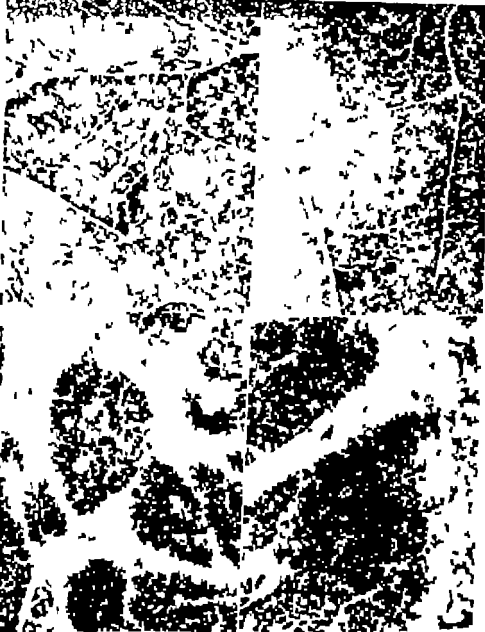


Fig. 2

Fig. 3

Fig. 1—Pumores of ex. 135, was star and, twenty-four hours, no then had separation  
 its exposure but not fixation of the pumores the ducts. Harvested forty-eight hours. It  
 hyperbolic

Fig. 2—Pumores from ex. 135 that had been starved twenty-four hours before the experi-  
 ment ducts showed no pumores the ducts less gth. Harvested forty-eight hours after the  
 that of the ducts

Fig. 3—First stage of pumores. Indication as described in text. Its width of  
 half degree. The ducts are secreted  
 in some distention of the ducts.  
 secondary reaction between the  
 a duct. There are two or three  
 critical forty-eight hours after harvest

TABLE I

NO OF CATS	DUCTS	FEED OR STARVED	INCUBATION	STIMULATION	T E CHOLINE	GRADE			
						1	3	4	
4	Exposed not tied	Starved	45 hr	None	0	0			
3	Exposed & tied	Fed	Died & operation	None	0	0			
4	Tied	Starved	45 hr	None	0	0			
	Exposed not tied	Fed	9 days	Secretin	0	0			
4	Tied	Starved	4 days	Secretin	3	1	1	1	1
	Tied	Starved	4 day	$\Delta$ choline	2				
6	Tied	Fed	4 hr	Secretin	5	1			3
8	Tied	Fed	45 hr	$\Delta$ choline	8	3			3
				secretin					
6	Tied	Starved	45 hr	Pilocarpine	6	2	1	1	
	Exposed not tied	Starved	45 hr	Pilocarpine	0	0			
17	Tied	Fed	45 hr & 6 days	None	14		4	6	6
6	Tied	Fed by tube after operation	45 hr	None			3	2	1

ducts were tied and the animal were fed or the stimulant administered, gross fat necrosis was found in the majority of the animals as noted in Table I. The amount of fat necrosis varied greatly. In the last inolved a few scattered areas were found along the mesentery of the pancreas and omentum. The animals with greatest involvement showed a wide distribution of fat necrosis in the omentum, and throughout the mesentery of the intestines and stomach. Between these two extremes were all degrees of this type of lesion. The pancreas from animal that had ligation of the duct and stimulation by feeding secretin, or other drugs showed on a microscopic section an inflammatory reaction which varied widely in degree. This inflammatory process seems to lend itself to classification in four categories.

1. The mildest degree of pancreatitis noted is a widening of the septa with presence of inflammatory cells and vacuolate in the septa. The pancreatic tissue appears just normal (Fig. 3).

The next stage shows a more extensive inflammation in the septa and beginning invasion of the lobules by inflammatory cells (Fig. 4).

3. In addition to these changes, the third stage reveals a beginning destruction of acini. This is most pronounced at the periphery of the lobule but occasionally seen in the center of the lobule (Fig. 4).

4. At this stage the entire lobule is undergoing dissolution and replaced by inflammatory cells (Figs. 5 and 6).

In the peritoneal cavity after forty-eight hours, one finds the inflammatory process proceeding to organization with fibroblastic proliferation. The amount of fibrous tissue laid down is commensurate with the previous destruction. It follows the lines of the previous inflammation one sees the greatest amount of fibrous tissue around the periphery of the lobules.



Fig 7

Fig 8

Fig 8—Stage 4, here the entire tubule is undergoing dissolution and acute inflammation. Very reaction is everywhere to be seen. Arrows and ducts in red, and animal material (early) high below later.

Fig 9—High-power view of Fig 8. ————— note slight hours after ligation of and given acetylcholine and darkened after ducts were

In the experiments with pilocarpine, acetylcholine, and eserine, where starved animal was used a few areas of fat necrosis were found and scattered areas of acute inflammation with destruction of pancreatic lobules were observed. Otherwise the gland appeared quite normal. This contrasts sharply with the fed animal and those that were given secretin. In these there was some inflammation throughout the entire gland with scattered foci of marked damage or complete destruction.

Vascular lesions were not found in most of our sections, but there were patchy areas of hemorrhage mingled with the inflammatory reaction in some of the gland. These areas were noted only in those with grade 3 and 4 in development. Some sections reveal damage to the wall of the blood vessels with destruction of the muscularis as noted by Rich and Duff. However we did not obtain extensive vascular damage as seen in human patients.

Failure to obtain gangrenous pancreatitis and extensive vascular damage puzzled us, but we believe that a probable explanation for this failure is the anatomy of the cat pancreas. The gland in the cat is thin and relatively free as compared with the human pancreas, which lies against the posterior wall of the lesser peritoneal cavity in a fairly snug connective tissue compartment. In the cat any internal pressure of secretion can force the juice to the surface quite readily, whereas, in the human being the thickness of the gland and its dense capsule allow the extruded secretion to remain longer in the gland substance before reaching the surface. The resultant autodigestion would therefore be more intense in the human being. There is very little fatty tissue within the cat's pancreas, whereas the human being presents many islands of fat cells. We found that the worst damage to the pancreatic tissue was usually adjacent to an area of fat necrosis on the surface of the gland.

#### DISCUSSION

One can produce inflammatory lesions of the pancreas and fat necrosis by ligating the duct in starved animal and then stimulating the gland by artificial means. But the most consistent and extensive inflammatory changes follow ligation of the duct at the height of digestion or about two hours after the animal has eaten.

Are the changes we have produced necessarily the same as those of acute pancreatitis in human beings? The pathologic distribution of severe lesions is quite characteristic of acute pancreatitis and the finding of normal lobules alongside those that are badly damaged is a common one. Eggers<sup>14</sup> reported a very interesting feature of acute pancreatitis in which there were many normal areas of gland tissue. The necrosis and inflammation proceeded along the interlobular septa and attacked the periphery of the lobules first. This same picture was found in our experiment. Reconstructing the sequence of events on the basis of the four degrees of pancreatitis in development noted in our animal work we think of this order. The pancreas secretes actively and suddenly the duct is obstructed. The pancreatic juice ruptures the duct which runs along the interlobular septa and initiates an inflammatory



reaction as the result of tissue damage. If the secretory pressure and enzyme concentration are not great, the process may end at this stage but if the secretory pressure is high or the enzymatic content of the juice is high, the autodigestion of tissue proceed to an attack of the gland on the periphery of the lobules as well as a penetration into the lobules. The patchy distribution of severe lesions can readily be explained by the location of the ductal rupture. Certainly the ducts will not rupture throughout their entire length, but rather in a few places. Wherever they rupture, the pancreatic juices will escape and produce local damage of an intensity commensurate with the volume and enzyme content of the extruded secretion.

In the light of these experiments most of the experimental and clinical fact can be rationalized. The occurrence of acute pancreatitis after a heavy meal at the height of digestion has been noted by clinicians for years. This is the time when the pancreatic juice contain the greatest concentration of enzymes. An obstruction of the gland at this time will thus cause the greatest autodigestion and tissue damage.

What causes the obstruction of the pancreatic duct in the human being? Mechanical factors such as stones and ascari at the ampulla have been summarized by Ravdin and Johnston. Archibald argued that in the absence of such elements, edema and spasm of the sphincter of Oddi could produce obstruction. He observed this spasm in cat. With the pressure in the biliary tree kept constant by a manometer the fluid was seen to enter the duodenum at interval rather than as a constant flow. In the light of clinical studies with tubes in the common duct this seems quite reasonable. Best and Hagen<sup>21</sup> found marked elevation in the intraductal pressure after cholecystectomy and they found that spasm of the sphincter could be relieved although temporary obstruction. McGowan, Butsch, and Walters<sup>22</sup> reported a marked increase in bile pressure along the common duct after morphine sulfate had been given, indicating mechanical blockage by spasm. This was relieved by glycerol trinitrate. Ivy and Sandbloom<sup>23</sup> showed that blockage of the biliary passage by spasm is possible in normal human subject and that magnesium sulfate placed in the duodenum relieves this spasm in a few minutes. A blockage of the bile passages at the ampulla will also obstruct pancreatic secretion. That spasm of the smooth muscle about the duct may be responsible in acute pancreatitis is suggested by Elman,<sup>24</sup> who noted that glycerol trinitrate placed under the tongue shortly after an acute attack of pancreatitis has begun would lead to a dramatic shortening of the attack.

This relief by glycerol trinitrate may not be the entire to relief of spasm in the sphincter of Oddi. It may also relieve spasm of the pancreatic ducts. In this connection one has published some significant but seldom quoted experiment on pancreatic secretion. This investigator studied the simultaneous changes in the size of the pancreas and secretory rate during vagal stimulation. During early stimulation of the vagus the pancreas increased in size. At first there was no secretion of juice but as the stimulation progressed the juice began to flow slowly and to increase gradually until it was

running at a steady rate through the cannula. Simultaneously with the flow went a subsidence of the glandular edema, and at the height of secretion the gland had returned to its original size.

Edema of the pancreas under normal conditions is a temporary stage associated with vagal stimulation. This edema may be due to secretion retained in the cells or to spasm of the duct. The normal reflex, when pushed beyond physiologic limits, could provide complete obstruction to pancreatic secretion being elaborated in the gland and a resultant backflow into the intercellular spaces.

A further possible mechanism of obstruction is edema of the duodenal mucosa. In patients who have overindulged in alcoholic beverages, hyperemia and edema of the duodenal mucosa are common findings. The opening of the bile and pancreatic ducts into the lumen are very small and could be closed temporarily by such swelling. Liebhafeld demonstrated this clearly in his experimental work. Alcohol is a stimulant of both gastric and pancreatic secretion and any obstruction of the pancreatic ducts occurring after ingestion of this agent would lead to the development of pancreatitis. The relation of alcoholism to clinical pancreatitis has been reported by Myers and Keefer.

The cause of obstruction in patient with gallstones who do not have a stone impacted at the ampulla is not entirely clear. The most obvious explanation at hand is that in such patient spasm of the pancreatic ducts or the sphincter of Oddi is much more readily produced than in normal patients. Wangensteen and associates furnish some suggestive evidence for this view. These investigators were unable to produce mechanical blockage of the bile and pancreatic duct by spasm in normal cats. They were however successful in producing obstruction by spasm in one animal that had an established infection of the gall bladder.

The degrees of pancreatitis seen clinically depend on many variables. The combination of obstruction and secretion may occur at different stages of the digestive process. The obstruction may be subacute or total. It may occur at the height of secretion or at the end.

For minimal pancreatitis or the edema as described by Florman we can assume either temporary obstruction or total obstruction with minimal secretion. In more advanced stages the obstruction is prolonged. When lesions of the blood vessels or of the obstruction has not only been of considerable duration but also the secretion has a goodly amount of proteolytic enzymes. The rare case of pancreaticoplex occurs when sudden complete obstruction develops at a secretion that is copious and rich in digestive enzymes.

#### SUMMARY

Experiment 1 and 2 have indicated some of the etiology of acute pancreatitis as has been reviewed.

Experiment has been reported of aut pancreatitis inflammation and fat necrosis produced by closing the pancreatic duct and stimulating the pancreas. Stimulation of the pancreas has been produced by (1) feeding (2) net lebolone and eserine (3) pilocarpine (4) irritation of the vagus. And

(5) secretin. In a high percentage of these experiments, combining obstruction of the pancreatic ducts and stimulation of the gland, acute inflammation of the pancreas and fat necrosis resulted. The most extensive and consistent damage resulted when the animals were fed two hours before ligation of the pancreatic ducts. The different mechanisms that can produce obstruction of pancreatic secretion have been discussed.

The clinical and experimental evidence has been correlated to explain the varying degree of acute pancreatitis seen at operation or autopsy.

#### CONCLUSION

*Acute pancreatitis is the result of ductal obstruction in an actively secreting pancreas.*

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# A COMBINED ABDOMINOTHORACIC INCISION PARTICULARLY ADAPTED FOR USE IN TOTAL GASTRECTOMY AND ESOPHAGOGASTRECTOMY

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IN AN attempt to extirpate cancer of the stomach surgeons have become progressively bolder and more aggressive. The operation of total gastrectomy which a generation ago carried almost a prohibitive mortality has today become a relatively common procedure in good surgical clinics. It was first successfully performed in 1897 by Schlatte<sup>1</sup> and in 1898 the first successful total gastrectomy in America was performed in San Francisco by MacDonald.

In 1929 Finner and Rienhoff<sup>2</sup> reported sixty-two cases collected from the literature to which they added five cases of their own. Of these sixty-seven cases there were thirty-six deaths, a mortality rate of 53.8 per cent. Recently Longmire<sup>3</sup> recorded his experience with twenty consecutive transabdominal total gastrectomies in which he reported two deaths, a 10 per cent mortality rate. In this clinic since Jan. 1, 1947 fifteen total gastrectomies have been performed with one death. These operations have been done by several members of the surgical staff of the University Hospitals. Some of these operations were further complicated by requiring concomitant resection of the lower esophagus, spleen, pancreas, colon and other neighboring organs.

Although surgeons lately are reporting mortality rates in the area of 10 per cent for transabdominal total gastrectomy the transthoracic transdiaphragmatic approach for total gastrectomy and resection of the lower esophagus with esophageal junction is still associated with a formidable mortality rate. The first successful operation of this type was reported in 1942 by Meyer.<sup>4</sup> Later Sweet<sup>5</sup> in 1944 reported six deaths in thirteen patients operated upon. In summarizing his series in 1944 he reported seven deaths in a series of eighteen cases, a mortality rate of 38.8 per cent.

Since the major portion of a total gastrectomy with resection of the lower esophagus involves principally in abdominal direction and yet the esophagojejunal anastomosis must be performed in the chest it was felt that a combined abdominothoracic incision would offer the best approach for these cases. Especially is this true for those surgeons who by virtue of training and experience find it a hard work principally in the abdominal or military ground, and from customary position and situation at the operating table. A description of such an incision and our experience with it is the purpose of this communication. This incision has been employed principally in cases of total gastrectomy with resection of the lower esophagus. One additional patient is included in this series in whom the combined abdominal and thoracic incision was successfully utilized in the repair of large paraesophageal hernia.

Before the physiology of respiration was adequately understood, surgeons were loath to open the pleural cavity. Starvedel, in 1903 in an effort to remove the barrier of the costal margin in exposing the area of the esophageal hiatus, devised a complicated incision cutting the costal cartilages and reflecting the costal margin laterally as a flap without entering the pleural cavity.

Kirschner in 1920 described a combined abdominothoracic incision which he used in four cases which is quite similar in principle to the present-day combined abdominothoracic approach. His incision with the patient in the lateral decubitus position, began at the boundary of the proximal and middle third of a line connecting the xiphoid process and the umbilicus, extended obliquely downward and laterally to the left costal margin, then across the eighth costal cartilage and out into the seventh interspace to the angle of the scapula. The diaphragm was then lifted from the costal margin to the esophageal hiatus.

Obayashi in 1933, used a combined abdominothoracic incision with a vertical abdominal component for resection of high gastric lesions. Humphreys, in 1946 utilized a similar combined incision but with a transverse abdominal component for resection of high gastric and low esophageal neoplasms. Garlock also utilized a combined abdominothoracic incision for partial esophagogastricotomy. Harper<sup>1</sup> wrote of employing a combined abdominothoracic incision in approaching the organs of the upper abdomen entering the thorax through the bed of the resected ninth rib and employing only a short abdominal component to the incision. Recently, the use of a combined abdominothoracic incision of difficult splenectomies was described by Carter. In none of the previous reports, however, has this incision been described and utilized to provide first principally an abdominal dissection, with the idea of extending the horizon of total gastrectomy to include removal of additional segments of the lower esophagus.

#### TECHNIQUE

The patient is positioned prone on the operating table with a sandbag under the left side producing about a 10 degree elevation from the horizontal. A kidney brace is fastened on the right side of the table to hold the patient in position when the table is rotated late in the operation. The skin incision (Fig. 1) begins near the lateral edge of the right rectus muscle slightly above the umbilicus and extends horizontally and upward to the left costal margin where the eighth costal cartilage crosses the seventh interspace. The incision is carried through the abdominal wall into the peritoneal cavity. Abdominal exploration is carried out at this time and operability of the lesion determined. If a decision is reached with resection and at this point the operating table is rotated, elevating further the left side of the patient to 20 to 30 degrees from the horizontal. The eighth costal cartilage is cut and the incision is extended into the pleural cavity through the seventh interspace as far as the mid or posterior axillary line. If total gastrectomy alone with infradiaphragmatic esophagojejunostomy is to be performed, incision of the diaphragm about halfway from the costal margin to the esophageal hiatus is carried out (Fig.

) If an additional segment of the esophagus is to be resected the diaphragmatic incision is continued to the esophageal hiatus (Fig 3). The left phrenic nerve as it passes along the lateral surface of the pericardium, is crushed early in the operation. This reduces motion of the diaphragm and aids in its subsequent repair and healing.

Dissection of the stomach particularly around the cardia and high along the lesser curvature in the area of the left gastric artery is markedly facilitated by removing the barrier of the costal margin. The abdominal portion of the operation, dissection of the lower stomach, transection of the duodenum and duodenal closure are readily accomplished. Mobilization of a jejunal loop for esophageal anastomosis is facilitated and if necessary one can readily section



Fig. 3—Skin incision

one or more of the mesenteric vessels near their origin to gain added mobility of the jejunal loop as recommended by Sweet. In performing the esophago-jejunal anastomosis, the technique of Wangensteen whereby the posterior side of the anastomosis is buttressed by two layers of interrupted silk sutures, starting along the mesenteric border of the jejunum, was regularly employed. All portions of the operation are performed without limitation of exposure. Because of the added exposure a wide and more complete excision of lymphatic-bearing tissue can be accomplished. Although the incision opens two serous cavities it is felt that the added exposure gained allows for a more careful dissection, preparation, and anastomosis so that leakage and infection which

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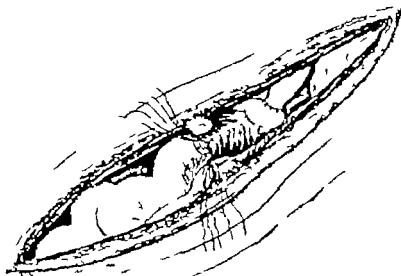


Fig. 4.—Closure of diaphragm diaphragm sutured to jejunal loop. The most anterior suture is tied until ribs are perforated. Then placed from the peritoneal surface and 4 times the beneath part of the incision after the intercostal incision is closed.

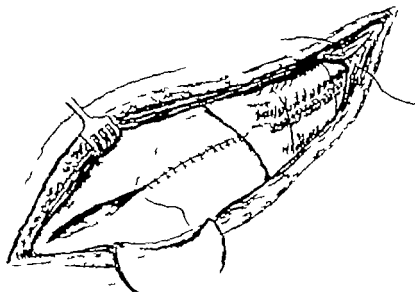


Fig. 5.—Closure of the peritoneal layer after the thoracic space is closed.



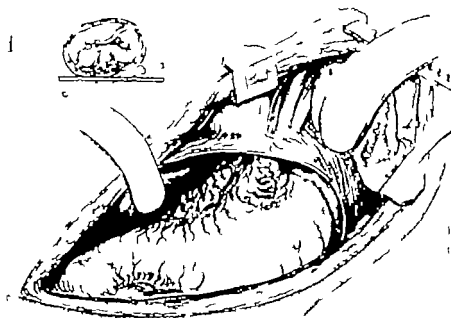


FIG. 2.—Incision opened. Its diaphragm incised part, as to the pleural space. Inset shows position of patient on the table. Its standing under the left side. Dashed line shows rotation of table and patient prior to making intercostal part of the incision.

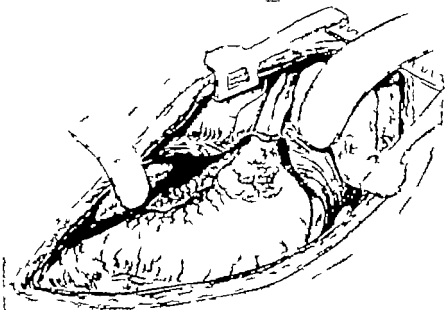


FIG. 3.—Exposure obtained with diaphragm incised to pleural space.

TABLE I. SUMMARY OF CASES IN WHICH THE ABDOMINOTHORACTIC INCISION HAS BEEN USED

CASE	TEST	AGE (YR.)	DISEASE	OPERATION	POST OPERATIVE COURSE	REMARKS
1	J. T. (U. S. N. 775170)	46	Carcinoma of upper stomach and lower esophagus	Subtotal gastrectomy and splenectomy; esophagectomy; intra-thoracic esophagojejunostomy	Left hospital on 9th postoperative day	Returned to hospital on 4th day after leaving, with mesenteric thrombosis; expired
2	U. M. (U. S. N. 76433)	41	Carcinoma of per stomach	Total gastrectomy with intra-thoracic phragmatic esophagojejunostomy	Left hospital on 10th postoperative day	No complications
3	M. U. (U. S. N. 774774)	4	Carcinoma of upper stomach	Total gastrectomy splenectomy; intra-thoracic phragmatic esophagojejunostomy	Left hospital on 8th postoperative day	No complications
4	J. B. (U. S. N. 43178)	52	Gastritis, chronic hypertrophic; polycythemia, choleliths chronic	Total gastrectomy, cholecystectomy intra-thoracic esophagojejunostomy	Left hospital on 15th postoperative day	Developed acute postoperative psychosis; no wound complications
5	C. R. (U. S. N. 774601)	—	Carcinoma of cardia of stomach with extension to pancreas	Total gastrectomy with resection of 3 cm. of esophagus, splenectomy pancreatotomy esophagojejunostomy	Left hospital on 8th postoperative day	No complications
6	G. A. (U. S. N. 774827)	67	Carcinoma of cardia of stomach and esophagus	Total gastrectomy partial esophagotomy splenectomy intra-thoracic esophagojejunostomy	Left hospital on 10th postoperative day	No complications
7	J. D. (U. S. N. —)	—	Recurrent carcinoma of residual gastric pouch gastric resection done 3 yr. previously extensive carcinoma of transverse colon and pancreas, cyst liver	Total gastrectomy resection of segment of colon, jejunum, pancreas, and cyst liver; intra-thoracic phragmatic esophagojejunostomy	Died on 8th postoperative day	At post mortem extensive suppuration pancreatitis and peritonitis were found; all metastases were intact
8	L. P. (U. S. N. 77100)	3	Upper paraesophageal hernia gastric bleeding	Repair of paraesophageal hernia from above; exploratory laparotomy	Left hospital on 5th postoperative day	No complications
9	M. J. (U. S. N. 477)	7	Carcinoma of cardia of stomach and lower esophagus	Subtotal gastrectomy and esophagectomy intra-thoracic esophagojejunostomy	Left hospital on 11th postoperative day	No complications
10	J. I. (U. S. N. 7778)	—	Carcinoma of cardia of stomach and lower esophagus	Subtotal gastrectomy and esophagectomy intra-thoracic esophagojejunostomy	Carotid artery left hospital on 6th postoperative day	—

Abdominostomy incision in the right flank. In the U. S. Navy, the other performed operations herein reported.

has been the principal cause of fatal outcome in most reported cases, are less likely to result. Resection of an added segment of esophagus, in doing a total gastrectomy is readily accomplished with the exposure obtained, whereas in doing a transabdominal total gastrectomy one cannot with ease sacrifice more than small segments of the esophagus.

Closure of the intercostal incision is shown in Figs 4 and 5. The diaphragm is circumferentially sutured to the anastomotic jejunal loop to prevent any herniation of abdominal viscera into the thoracic cavity. The last few anterior sutures in the diaphragm are placed from the peritoneal surface and tied later from below after the intercostal incision has been closed. In two areas the rib above and below the incision is bared of periosteum, and perichondral sutures of 0 chrome catgut are passed around the ribs, care being taken to avoid cutting the intercostal nerves. Tying of these sutures closes the intercostal space. This is further closed by interrupted 000 or 0000 silk sutures uniting the cut intercostal muscle bundles. This is reinforced by suturing the serratus anterior muscle.

The abdominal component of the incision is closed in the usual fashion, using interrupted 000 silk in the peritoneal layer and in the anterior rectus sheath. Because of the length of incision the closure takes considerable time. This can be shortened by having two closure teams working from either end toward the center.

Table I presents in summary our experience with the combined abdomino-thoracic incision in ten cases. In all, excellent exposure for all phases of the operation was obtained. No complications attributable to the incision were noted. In those cases in which supradaphragmatic esophagojejunal anastomosis was performed, closed intercostal catheter drainage of the pleural cavity was employed for several days postoperatively. In the cases where infradiaphragmatic anastomosis was employed, pleural drainage was used. One death occurred in a patient (Case 7 Table I) with recurrent carcinoma of the stomach, in whom an extensive operation was necessary to remove the neoplasm. The fatal outcome resulted from pancreatitis and peritonitis and was unrelated to the incision which had greatly facilitated a long and difficult operation. Although the incision has been used principally for total or subtotal gastrectomy with resection of the lower esophagus, the report of one additional patient (Case 8 Table I) in whom it was successfully utilized for the repair of a large para-esophageal hernia, is too brief to detail.

Two potential disadvantages to the incision should be pointed out. First, unless the patient is rotated somewhat laterally there is a tendency for the heart to interfere with exposure in making high esophagojejunal anastomosis above the diaphragm. Second, with this exposure one is limited to dissection of the esophagus below the hilum of the lung and the inferior pulmonary hilum. Above this point the esophagus is posterior to these structures and cannot be adequately exposed. An esophageal anastomosis must therefore be done below the hilum of the lung. This circumstance precludes the use of this incision for resection of lesions in the mid-esophagus, and, in any event, where one expects that more than the lower one fourth of the esophagus is to be sacrificed. It is

## GASTRIC RESECTION THE SCHOEMAKER BILLROTH I OPERATION

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THE purpose of this presentation is to consider (1) the Schoemaker modification of the Billroth I operation, (2) some of the reasons why when feasible, this operation seems better than the Hoffmeister Polya operation in which the treatment of the stomach is the same but reconstruction of continuity of the intestine is different, and (3) the immediate results in ninety five cases in which the Schoemaker Billroth I technique has been used.

The Schoemaker modification of the Billroth I operation permits greater, more extensive, resection of the lesser curvature of the stomach than other similar operations. After resection it provides for closure of this portion of the open end of the stomach, thereby producing a tubelike stomach with a stoma at the greater curvature aspect. This stoma is utilized in end-to-end anastomosis to the duodenum.

In other modifications of the Billroth I operation, as well as the original operation as described by Billroth, either the entire end of the remaining portion of the stomach is utilized for the gastroduodenostomy or less extensive resection of the lesser curvature of the stomach is carried out before closing this superior portion of the site of transection. The Schoemaker modification will permit resection along the lesser curvature to the esophagus, and even slightly into the wall of this latter structure if necessary and yet will leave sufficient stomach to perform a gastroduodenostomy.

These advantages of the Schoemaker modification of the Billroth I operation are the same exactly as result with the use of the Hoffmeister Polya technique.

The chief reason lies in the reconstruction of the continuity of the intestine. When it is feasible gastroduodenostomy or in other words completion of the operation in the Billroth I manner seems better than, and preferable to gastrojejunostomy. The former results eventually in greater comfort and better more efficient physiologic activity.

Wollaeper, Comfort, Weir and Osterberg studied a group of patients who had had partial gastrectomy with a full Polya anastomosis and found an excessive loss of fat and nitrogen in the feces, which caused a decrease in body weight unless diet of sufficient caloric content was taken to compensate for the wasteful loss. These authors noted that patients who had mild or no digestive symptoms tended to lose less fat in the feces than did the patients who had severe digestive symptoms. Some of the more important possible factors which they considered accountable for the excessive loss of fat and nitrogen in the stools of persons who had undergone partial gastrectomy with a Polya anastomosis were (1) rapid emptying of the stomach, (2) intestinal hurry, (3) diminished flow of pancreatic secretions or bile because of impairment of the mechanism of stimulation of such flow and (4) imperfect mixing of food with digestive ferments because of the shunting of gastric contents away from the duodenum.

Received for publication, Oct. 23, 1931.

especially useful for high gastric lesions where invasion of the lower esophagus has occurred and where in addition to resection of the stomach one wishes to resect more of the esophagus than one can conveniently do by the transabdominal approach alone.

## SUMMARY

A description of an experience with a combined abdominothoracic incision especially as it relates to use in total gastrectomy and esophagogastronomy is presented. The incision has been employed in ten instances with excellent exposure, greatly facilitating a difficult operation. No untoward effects or complications have attended its use.

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## GASTRIC RESECTION THE SCHOEMAKER BILLROTH I OPERATION

JOHN F. HOGGEBSON, M.D. AND O. THERON CLAGETT, M.D. ROCHESTER, MINN.

(From the Division of Surgery, Mayo Clinic)

THE purpose of this presentation is to consider (1) the Schoemaker modification of the Billroth I operation, (2) some of the reasons why when feasible this operation seems better than the Hoffmeister Polva operation in which the treatment of the stomach is the same but reconstruction of continuity of the intestine is different, and (3) the immediate results in ninety five cases in which the Schoemaker Billroth I technique has been used.

The Schoemaker modification of the Billroth I operation permits greater more extensive resection of the lesser curvature of the stomach than other similar operation. After resection it provides for closure of this portion of the open end of the stomach, thereby producing a tubelike stomach with a stoma at the greater curvature aspect. This stoma is utilized in end to-end anastomosis to the duodenum.

In other modifications of the Billroth I operation as well as the original operation as described by Billroth, either the entire end of the remaining portion of the stomach is utilized for the gastroduodenostomy or less extensive resection of the lesser curvature of the stomach is carried out before closing this superior portion of the site of transection. The Schoemaker modification will permit resection along the lesser curvature to the esophagus, and even slightly into the wall of this latter structure if necessary and yet will leave sufficient stomach to perform a gastroduodenostomy.

These advantages of the Schoemaker modification of the Billroth I operation are the same exactly as result with the use of the Hoffmeister Polva technique.

The difference lies in the reconstruction of the continuity of the intestine. When it is feasible gastroduodenostomy or in other words completion of the operation in the Billroth I manner seems better than, and preferable to, gastrojejunostomy. The former results eventually in greater comfort and better more efficient physiologic activity.

W. Haeger, Comfort, Weir and Osterberg studied a group of patients who had had partial gastrectomy with a full Polva anastomosis and found an excessive loss of fat and nitrogen in the feces, which caused a decrease in body weight unless a diet of sufficient caloric content was taken to compensate for the wasteful loss. These authors noted that patients who had mild or no digestive symptoms tended to lose less fat in the feces than did the patients who had severe digestive symptoms. Some of the more important possible factors which they considered accountable for the excessive loss of fat and nitrogen in the stool of a person who had undergone partial gastrectomy with Polva anastomosis were (1) rapid emptying of the stomach, (2) intestinal hurry, (3) diminished flow of pancreatic secretions or bile because of impairment of the mechanism of stimulation of such flow and (4) imperfect mixing of food with digestive ferments because of the shunting of gastric contents away from the duodenum.

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The edges of the stomach transected by the pin of the Furniss clamp are united by means of an overlapping hemostatic suture (Fig 2, a). The pin is removed and the suture is returned to the starting point as an inverting suture. A row of interrupted silk serosal sutures is then used for further reinforcement.

A rubber-covered clamp is then placed just proximal to the remaining curved clamp and the latter is cut free with its contained, crushed bit of gastric tissue.

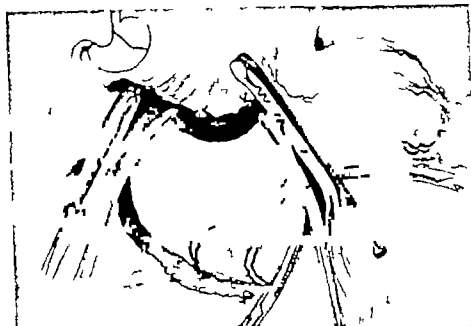


Fig. 1.—Rubber-covered clamp is placed across the duodenum just distal to the pylorus and the duodenum is transected. Curved clamps are placed parallel to each other on the lesser curvature and the stomach cut between them to their tips. A Furniss clamp is placed obliquely across the stomach pointing up along the lesser curvature, another curved clamp is placed just distal to the Furniss clamp, and the stomach is removed.

The two rubber-covered clamps, the one holding the duodenum and the other the pylorus and the stomach, are then approximated for the anastomosis. Usually the lumen of the duodenum is smaller and must be fitted to the slightly larger gastric stoma. This bit of custom tailoring is achieved by means of a continuous posterior serosal silk suture which begins and ends on the duodenum and which, on being pulled tight, neatly approximates the two orifices (Fig 2, b and c). The rest of the anastomosis is completed in a standard manner with two rows of catgut posteriorly and anteriorly and interrupted silk serosal sutures anteriorly. The superior wall is reinforced by approximating the serosa of the upper aspect of the duodenum to the serosa of the posterior and anterior wall of the lower curvature of the stomach with one or two silk sutures. One of these latter is tied the upper end of the continuous posterior serosal silk suture the inferior end being similarly tied and anchored. A bit of omentum is usually pulled up posteriorly and sutured over the superior aspect of the anastomosis for further protection.



Our clinical impression is that patients who have had a Hoffmeister Polya anastomosis have less postprandial distress and less difficulty in gaining or maintaining body weight than patients who have had a full Polya anastomosis, and that patients who have had a Schoemaker Billroth I anastomosis do best of all. In fact patients in the last group do not seem to suffer from the so-called dumping syndrome to any appreciable degree.

Wollaeger and Comfort are concluding a study of intake and excretion on a group of patients on whom the Hoffmeister Polya anastomosis was used, and also on a group on whom a Schoemaker Billroth I anastomosis was done. Although their work has not been fully studied and the data evaluated as yet the results of their studies seem to support our clinical impression.

#### TECHNIQUE

The essential of the technique of the Schoemaker Billroth I operation concerns the delimitation of the resection and the closure of part of the stomach in order to form a tube of stomach which can be used in the subsequent gastroduodenostomy.

On exploration of the lesion after the abdomen is opened, several factors must be noted to determine whether this technique can be used. This will depend, of course, on whether partial gastrectomy is indicated and the lesion is operable. These factors principally concern the duodenum, but unusual inflammatory fixation of the stomach especially of the portion remaining after resection, may prevent use of this technique. Considerable narrowing or stenosis of the duodenum or considerable inflammatory reaction and fixation of the duodenum will prevent gastroduodenostomy. Also, a duodenum which has been the site of peptic ulceration may be shortened so much that a gastroduodenal anastomosis may jeopardize the common bile duct since in some such instances the papilla of Vater is only 2 or 3 cm from the pylorus. Occasionally especially in obese patients, the uninvolved duodenum will lack sufficient mobility to permit gastroduodenostomy after partial gastrectomy of a gastric lesion.

Mobilization of the stomach with appropriate resection of omentum, mesocolon and so forth, when indicated, and with ligation of the various blood vessels is done in the usual manner. The duodenum is resected in an suitable and preferred manner but if gastroduodenostomy is planned, a rubber-covered intestinal clamp should be placed distal to the site of transection.

Whether a Schoemaker Billroth I or a Hoffmeister Polya operation is to be done the stomach is treated in exactly the same manner. At the elected site for transection two curved clamps are placed parallel to each other on the stomach, from the greater curvature roughly perpendicular to this edge of the stomach and the vessels cut between them.

From the tip of the proximal clamp to the lower curvature Furniss clamp (actually any type of clamp may be used) is applied obliquely to the esophago-gastric junction. The degree of obliquity varies with the amount of tissue on the lower curvature which it is desired to remove. Another curved clamp is applied just distal to the Furniss clamp to prevent spilling and this clamp is removed (Fig. 1).

This observation indicates, therefore, that the operation is most useful for gastric lesions. In so far as carcinoma of the stomach is concerned it might be argued that proximity of the carcinoma to the pylorus contraindicates the use of a gastroduodenostomy especially if there are enlarged nodes near the duodenum and head of the pancreas. It is our feeling that these factors are important only if resultant inflammatory reaction or carcinomatous extension has caused fixation and loss of mobility of the duodenum. As a matter of fact such involvement might in itself render inoperability in some instances.

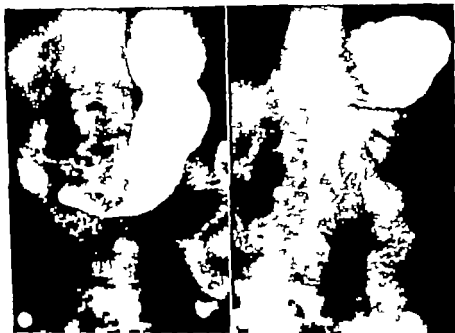


FIG. 3.—a. Preoperative appearance of the stomach of a woman 54 years old with an adenocarcinoma of the stomach. b. Postoperative appearance of the stomach of the same patient as localized on Feb. 25, 1948. There is no roentgenologic evidence of recurrence.

In eight-nine of the ninety-five cases, an estimation of the amount of stomach resected was recorded in numerical fractions. In sixty-four cases (72 per cent of the eighty-nine) the estimation was one-half, slightly more than one-half or three-fifths. In all ninety-five cases the resected portion of the stomach was measured along a line midway between the two curvatures. In sixty-nine (73 per cent) of these specimens the measurement was 1. to 15 cm.

These estimations and measurements must be considered in the light of differences in size of various stomachs, and, furthermore they are not truly indicative of the extent of resection of the lesser curvature. The Schoemaker technique with Billroth I anastomosis or the Hoffmeister technique with Polya anastomosis will permit as much complete resection of the lesser curvature, which feature is not revealed by the method of measurement employed.

In twenty cases (21 per cent) associated operations were performed (Table III).

## RESULTS IN NINETY-FIVE CASES

Of the ninety five patients in our group seventy-three were men; their ages averaged 55 years and ranged from 30 to 77 years. Twenty-two patients were women; their ages averaged 51 years and ranged from 27 to 76 years.

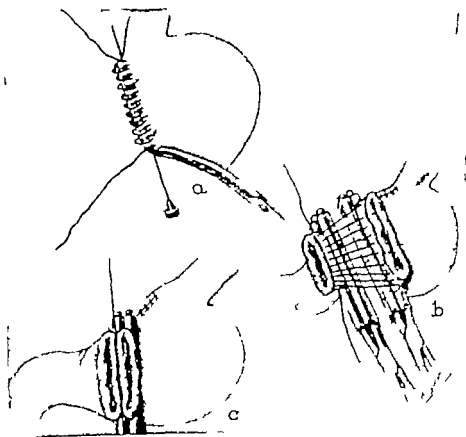


FIG. 2.—a, Lower early type portion of the end of the stomach is closed off, the jejunum is inserted into the duodenum and the duodenum is closed off the jejunum, the jejunum is closed off the duodenum.

Results obtained for an elderly woman who had adenocarcinoma are indicated in Fig. 3 a and b.

The conditions for which gastric resection was done are listed in Table I. In only three cases in which duodenal ulcer was the primary lesion was it possible to perform a Schoemaker Billroth I resection. Five patients had old or new duodenal ulcers accompanying more important gastric lesions (Table II). Accordingly this type of anastomosis was possible in the presence of duodenal ulcer (of primary or secondary importance) in only eight instances.

TABLE IV POSTOPERATIVE GASTRIC RETENTION IN SIXTEEN CASES

DURATION IN DAYS	CASE	POSTOPERATIVE DAY OF OCCURRENCE	EMESIS DURING OPERATION (CC IN 24 HRS.)	ADDITIONAL OPERATIONS
1	3	11 11 10	1,300 850 950	None
	4	and 3 3 and 4 4 and 5 7 and 9	8.5 273 1,700 930 400 430 200, 8.5	None
3	4	— 4 and 4 — 4, and 9 — 4 and 5 — 2, and 7	700 500 500 600 700, 300 50 1,050 100 400 950 600	None
7	1	First 7	Usually large	None
9	2	First 9	Usually large	1. A (terno gastroenterostomy and enteroenterostomy 3 weeks after resection in 1 case 2. Patient died with postoperative dyspnea and respiratory failure
12	1	First 6 11 1	Usually large	None
48	1	8 50	Usually large	Drainage of small subhepatic abscess and jejunostomy 2 weeks postoperatively anterior gastroenterostomy seven weeks postoperative

Day of surgery considered first postoperative day

(16.8 per cent) had significant postoperative gastric retention (Table IV). The vomiting of quantities of 100 cc or less during the first thirty-six or forty-eight hours after operation or a portion of such amounts in this period was not considered significant retention, nor was a single emesis of similar quantity considered to indicate retention even if occurring in the second week after operation. Significant retention was considered present if the vomiting of more than 100 cc of material occurred on one day or on several days, successive or not even if gastric aspiration after vomiting yielded no additional material.

In five of the sixteen cases the retention was of more than three days' duration. In four of these five cases retention began immediately after operation and in one on the eighth day (counting the day of operation as the first day). In eleven of the sixteen cases retention lasted three days or less. Those of one day's duration occurred on the tenth or eleventh day while the others occurred within the first week for the most part.

The other postoperative complications in this series of patients are listed in Table V.

TABLE V OTHER POSTOPERATIVE COMPLICATIONS

Complications	TOTAL NO.
Unfavorable complications	20
	11
	1
	2
	6

TABLE I. CO-EXTENSIVE LESIONS OF THE GASTRIC LESION

	Men	Women	Total
Peptic ulcer			
Duodenal	2	1	3
Gastric	30	7	37
Carcinoma of stomach	20	1	21
Chronic gastritis	4	0	4
Gastrojejunal ile	2	1	3
Multiple polyps of stomach	0	1	1
Lymphosarcoma of stomach	1	0	1
Adenocarcinoma, low-grade			
Adenoma of stomach	1	0	1
Inflammatory cyst of stomach			
from gall bladder	1	0	1
Total	73	22	95

Leakage at the site of anastomosis occurred in two cases, was probable in one more, and questionable in one. In the last case the leak was suspected because of the drainage around the Penrose drain, but this was so slight and transitory that the presence of a leak was questionable. The probable leak occurred in the case in which postoperative gastric retention lasted forty-eight days, and a right subhepatic abscess was drained three weeks after operation.

Of the two patients who had definite leaks, one died on the ninth postoperative day and at necropsy separation of the suture line was found with an old local abscess and recent general peritonitis. In the other case the familiar fistula and infected wound developed and endured for fourteen days before healing.

TABLE II. DUODENAL ULCERS

	Men	Women	Total
Duodenal ulcer			
Primary lesion	2	1	3
Accompanying gastric ulcer	9	1	10
Accompanying chronic gastritis	1	0	1
Total	6	2	8

Two hospital deaths (2.1 per cent) occurred in the series. One was the patient whose case was just described; the other patient died of a postoperative cerebrovascular accident. Both of these patients had had carcinoma of the stomach.

Although gastric retention developed in some of these cases as it does after other types of anastomosis, the retention was seldom severe or long lasting, and was easily controlled in most instances. Of the ninety-five patients, sixteen

TABLE III. ASSOCIATED OPERATION

Operation	No.
Appendectomy	1
Dissection of gastroenterostomy and closure of opening of jejunum, 2	
With splenectomy 1	4
Splenectomy and partial pancreatectomy	1
Cholecystectomy	2
Repair of postoperative atrial hernia	
Splenectomy and partial hepatectomy	1
Splenectomy and removal of gastric leiomyoma	1
Splenectomy	1
Removal of part of transverse colon and double barrel colectomy	1
Repair of operative hernia	1

TABLE IV POSTOPERATIVE GASTRIC RETENTION IN SIXTEEN CASES

DAY AFTER OPERATION	CASE	POSTOPERATIVE DAY OF ONSET	GASTRIC ASPIRATION (IN CC)	ADDITIONAL AFTER 1 HOUR
1	3	11 11 10	1,200 800 800	None
2	4	2 and 3 3 and 4 4 and 5 and 9	525, 775 1,700, 950 400, 430 200, 525	None
3	4	— 2, and 4 — 3, and 8 — 4 and 5 — 2, and 7	700, 500, 500 600, 200, 300 750, 1,050, 100 500, 250, 600	None
7	1	First 7	Usually large	None
8		First 8	Usually large	1. Anterior gastroenterostomy and entero- enterostomy 3 week after resection in 1 case. Patient died 10th postoperative day; separation of suture line.
1	1	First 6, 11, 1	Usually large	None
14	1	4th	Usually large	Drainage of small subpyloric abscess and pylorostomy 1 week postoperatively; anterior gastroenterostomy seven weeks postoperatively.

Day of surgery is considered first postoperative day.

(16.8 per cent) had significant postoperative gastric retention (Table IV). The vomiting of quantities of 100 cc or less during the first thirty-six or forty-eight hours after operation or apiration of such amounts in this period was not considered significant retention, nor was a single emesis of similar quantity considered to indicate retention when it occurred in the second week after operation. Significant retention was considered present if the vomiting of more than 100 cc of material occurred on one day or on several days, successive or not even if gastric aspiration after vomiting yielded no additional material.

In five of the sixteen cases the retention was of more than three days duration. In four of these five cases retention began immediately after operation and in one on the eighth day (counting the day of operation as the first day). In eleven of the sixteen cases retention lasted three days or less. Those of one day's duration occurred on the tenth or eleventh day while the others occurred within the first week for the most part.

The other postoperative complications in this series of patients are listed in Table V.

TABLE V OTHER POSTOPERATIVE COMPLICATIONS

Complications	TOTAL
Wound complications	29
—	11
—	1
—	2
—	3

Included

TABLE I. CONDITIONS FOR WHICH GASTRIC RESECTION WAS DONE

	MEN	WOMEN	TOTAL	PERCENT
Peptic ulcer				
Duodenal	2	1	3	10
Gastric	20	7	27	
Carcinoma of stomach	23	12	35	44
Chronic gastritis	4	0	4	4
Gastrojejunal ulcer		1	1	3
Multiple polyps of stomach	0	1	1	1
Lymphosarcoma of stomach	1	0	1	1
Adenocarcinoma, low grade 1				
in adenoma of stomach	1	0	1	1
Inflammatory cyst of stomach				
from gall bladder	1	0	1	1
Total	73	23	96	

Leakage at the site of anastomosis occurred in two cases was probable in one more and questionable in one. In the last case the leak was suspected because of the drainage around the Penrose drain but this was so slight and transitory that the presence of a leak was questionable. The probable leak occurred in the case in which postoperative gastric retention lasted forty-eight days, and a right subhepatic abscess was drained three weeks after operation.

Of the two patients who had definite leaks, one died on the ninth postoperative day and at necropsy separation of the suture line was found with an old local abscess and recent general peritonitis. In the other case the familiar fistula and infected wound developed and endured for fourteen days before healing.

TABLE II. DEATHS &amp; ULCERS

	NO.	PERCENT	TOTAL	PERCENT
Duodenal ulcer				
Primary lesion	2	1	2	2
Accompanying gastric ulcer	2	1	4	4
Accompanying chronic gastritis	1	0	1	1
Total	5	2	7	7

Two hospital deaths (1 per cent) occurred in the series. One was the patient whose case was just described, the other patient died of a postoperative cerebrovascular accident. Both of these patients had had carcinoma of the stomach.

Although gastric retention developed in some of these cases as it does after other types of anastomosis, the retention was seldom severe or long lasting, and was easily controlled in most instances. Of the ninety-five patients, sixteen

TABLE III. ASSOCIATED OPERATIONS

OPERATION	NO.
Liver resection	4
opening of jejunum, 3	4
	3
	2
	3
	1
	1
Hysterectomy	1
Resection of part of transverse colon and double barrel colectomy	1
Repair of epigastric hernia	1

## A SUCTION AND FEEDING TUBE FOR THE POSTOPERATIVE CARE OF GASTRIC RESECTIONS

LAWRENCE HINGMASTER, M.D. PHILADELPHIA, Pa.

(From the Surgical Service of Lankenau Hospital)

THE surgeon is confronted with two important problems concerning the immediate postoperative management of patients who have had gastric resections. The first problem is that of adequate intragastric drainage and decompression to prevent pressure at the line of anastomosis with the jejunum. The second problem is that of meeting the nutritional requirements of the patient until he can take adequate food by mouth.

A Levine tube with a Wangensteen suction apparatus attached will provide adequate drainage for these cases but the nutritional problem is still unsolved. Water, chloride, carbohydrate, and vitamins can be administered parenterally but protein intake is inadequate postoperatively despite advances in parenteral hydrolyzates.

Utilizing the principle of the double-barreled Abbott-Rawson tube, I have devised a simplified suction-feeding tube which has proved to be clinically effective in the postoperative treatment of gastric resections. The resections were performed at the Lankenau Hospital for gastric and duodenal ulcers and carcinoma of the stomach and in no instance has the tube caused untoward results.

The device is a size 16 French double lumen tube of soft rubber 50 inches in length. The distal end terminates in a hard rubber tip sealing a column of mercury within the tube for a distance of 3 inches from the tip. Just proximal to the sealed mercury column are perforations for feeding purposes. Thirteen inches proximal to the tip is another series of perforations for intragastric suction. The proximal end of the tube bears a double lumen metal connection, one lumen of which is marked "F" for feeding and the other lumen marked "S" for suction.

Accordingly, the feeding lumen terminates in the perforations at the end of the tube and is completely separate from the suction lumen which terminates in perforations well proximal to the tip. The tube is so divided that the suction lumen is of larger diameter than the feeding lumen, allowing adequate drainage of blood and gastric secretion postoperatively. The feeding lumen is ample for liquid protein preparation in a proper dilution.

Preoperatively the patient undergoing resection is prepared by draining and lavaging the stomach with tap water, a weak solution of bicarbonate of soda until the drainage return is clear. This can be performed the evening before operation with a Levine tube allowing the tube to drain by gravity.

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This suction-feeding tube is manufactured by George F. Ellis & Son Co., Philadelphia, Pa.



## COMMENT

The Billroth I types of gastric operation are the most logical in so far as reconstruction of continuity of the alimentary tract is concerned and, of these, the Schoemaker modification is one of the easiest to perform, permits wide resection when desired, and yields the most nearly natural gastroduodenal continuity and relationship.

The Billroth I type of gastric operation has been much neglected in favor of the Polya forms of the Billroth II type. This neglect is largely the result of operations for duodenal ulcer for which only a Billroth II type of anastomosis is possible in most instances. However it also has resulted from the general use of the full Polya anastomosis in cases of gastric carcinoma as well as duodenal ulcer. In this procedure the straight-across transection and use of the full mouth for anastomosis make a gastrojejunostomy almost mandatory. Only occasionally can a von Haberer Billroth I operation be done with such a gastric stump and then only if the duodenum is unusually large and mobile.

It is naturally true, and obvious, that a Schoemaker Billroth I operation cannot always be done because of a fixed or immobile duodenum, a fixed stomach, a stenosed or inflamed duodenum, or because resection along the greater curvature of the stomach is of necessity high. However the various duodenal and gastric features must be evaluated and considered in each case. This is well illustrated in the extreme in those cases in which esophagoduodenostomy has been possible after total gastrectomy.

From a physiologic standpoint the narrow stoma of a Schoemaker Billroth I or a Hoffmeister Polya anastomosis seems better than the wide stoma of a full Polya anastomosis. The Schoemaker Billroth I anastomosis seems better than the Hoffmeister Polya. The small stoma and the reconstruction of normal continuity by gastroduodenostomy seem to return the duodenum and stomach as nearly as possible to normal physiologic activity.

It might be argued that the small stoma resulting from use of the Schoemaker Billroth I or the Hoffmeister Polya technique predisposes to a greater incidence of postoperative gastric retention than does the larger stoma of the posterior Polya operation. It is possible also that this is more marked after the Schoemaker Billroth I operation than after the Hoffmeister Polya.

If, however, clinical impressions as to comfort, maintenance of body weight, and degree of postprandial distress are confirmed by factual laboratory studies (as they seem to be so far) then the order of preference when possible would seem established for these methods of gastric resection.

## REFERENCES

## A SUCTION AND FEEDING TUBE FOR THE POSTOPERATIVE CARE OF GASTRIC RESECTIONS

LAWRENCE SINGMASTER, M.D. PHILADELPHIA, PA.

(From the Surgical Service of Lankenau Hospital)

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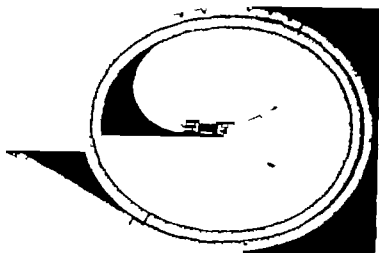
Suction. Accordingly the feeding lumen terminates in the perforations at the end of the tube and is completely separate from the suction lumen which terminates in perforations well proximal to the tip. The tube is so divided that the suction lumen is of larger diameter than the feeding lumen allowing adequate drainage of blood and gastric secretions postoperatively. The feeding lumen is ample for liquid protein preparations in a proper dilution.

Preoperatively the patient undergoing resection is prepared by draining and lavaging the stomach with tap water. A weak solution of bicarbonate of soda until the drainage returns is less. This can be performed the evening before operation with a Levine tube allowing the tube to drain by gravity.

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\*The suction-feeding tube is manufactured by George F. McKim & Son Co., Philadelphia, Pa.

until the morning of operation. At this time the Levine tube is removed and the suction feeding tube may then be passed through the nose and pharynx. The passage of the tube through the nose is easily effected without injury to the mucosa and is facilitated by using a lubricant such as mineral oil. There is no tendency for the tube to coil back into the mouth owing to the weight and rigidity of the tip provided by the sealed column of mercury. The tube is then passed down the esophagus until the 18 inch mark is reached, at which point the tip lies just within the stomach. The tube is then secured with tape at the nose to prevent further movement.



Levine tube in situ

The surgeon proceeds with the gastric resection and upon completing the posterior row of mucosal sutures of the anastomosis, the suction-feeding tube is freed at the nose and advanced further by the anesthetist. The tip is then grasped by the surgeon, using a Babcock or Allis lamp and is introduced into the efferent loop of jejunum. Continuing to advance the tube through the nose and guiding the tube through the anastomosis, the tip is advanced 13 inches into the jejunum. At this point the suction perforator appears and these should be allowed to lie just proximal to the line of anastomosis. The tube is secured again at the nose and the intubation is completed. Any looping of the tube which might occur as it passed down the jejunum can be easily controlled by the assistant surgeon.

The anastomosis is then completed and the efferent loop of jejunum tends to fall away from the liver owing to the presence of the lying tube. This

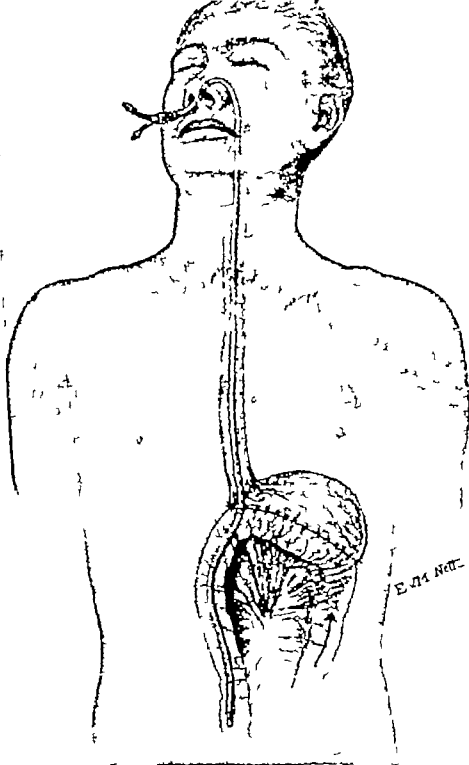


Fig. —Diagram showing tube in place after operation. The air perforations lie well down the abdominal cavity of jejunum or alimentary passage and the proximal perforations lie the line of anastomosis for decompression and suction.

until the morning of operation. At this time the Levine tube is removed and the suction feeding tube may then be passed through the nose and pharynx. The passage of the tube through the nose is easily effected without injury to the mucosa and is facilitated by using a lubricant such as mineral oil. There is no tendency for the tube to coil back into the mouth owing to the weight and resiliency of the tip provided by the sealed column of mercury. The tube is then passed down the esophagus until the 18 inch mark is reached at which point the tip lies just within the stomach. The tube is then secured with tape at the nose to prevent further movement.

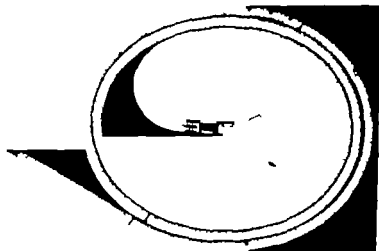


Figure of discal  
dial tip are  
are 1 inch  
in 1 inch

The surgeon proceeds with the gastric resection and upon completing the posterior row of mucosal sutures of the anastomosis, the suction-feeding tube is fixed at the nose and advanced further by the anesthetist. The tip is then grasped by the surgeon, using a Babcock or Allis clamp and is introduced into the efferent loop of jejunum. Continuing to advance the tube through the nose and guiding the tube through the anastomosis, the tip is advanced 18 inches into the jejunum. At this point the suction perforations appear and these should be allowed to lie just proximal to the intestinal anastomosis. The tube is secured again at the nose and the intubation is completed. Any looping of the tube which might occur as it is passed down the jejunum can be easily controlled by the assistant surgeon.

The anastomosis is then completed and the efferent loop of jejunum tends to fall away from the liver owing to the presence of the milking tube. This

# DIAPHRAGMATIC HERNIA FOLLOWING SUBDIAPHRAGMATIC VAGOTOMY

## A CASE REPORT

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THE present interest in section of the vagus nerves in the treatment of peptic ulcer and the increasing number of articles on the subject found in the literature may justify the report of an unusual complication—a diaphragmatic hernia following subdiaphragmatic vagotomy.

In a recent article Moses<sup>1</sup> reviewed the complications of vagotomy. The majority of the undesirable sequelae have been due either to incomplete section of the vagus nerves with failure to abolish the cephalic cause of gastric secretion, or to unpleasant physiologic side-effect accompanying the division of these nerves. The most frequently recorded of the latter are disturbances in gastric motility as evidenced by belching, fullness, loss of appetite, and vomiting.<sup>2,3</sup> Diarrhea is not infrequently experienced by patients following vagotomy. Dragstedt and associates<sup>4</sup> stated that prolonged gastric suction followed by slow progression of the diet postoperatively will largely overcome the gastric atony and consequent symptoms. Our experience has tended to confirm these findings.

Obstipation was encountered by Moses in one instance, relief being obtained by bronchial block of the celiac ganglion. Carlson<sup>5</sup> reported temporary stenosis of the esophagus at the level of resection of the vagus nerves, but a search through the literature failed to reveal diaphragmatic herniation as a complication of vagotomy.

A case of diaphragmatic herniation following vagotomy is summarized here.

## CASE REPORT

C. P. (N. Y. H. N. 49067)—A 34-year-old American married man, a construction worker, 37 years of age, as admitted to the surgical service of the New York Hospital Oct. 1, 1947 complaining of epigastric pain of three weeks' duration.

The patient had the onset of ulcer-type pain fifteen years previously and duodenal ulcer was demonstrated by roentgen examination at that time. He was treated by diet, by medication and by sympathectomy for ten years.

Five years prior to the admission he began to have bouts of epigastric pain relieved by milk and meals or alkali, recurring every six months and lasting about three weeks. Two years later he hadarry stool for three days during an exacerbation of pain. Three weeks before admission he had the onset of epigastric pain radiating through to the back and nausea. The pain progressed in severity and he vomited at times during this period. No bloody or tarry stools, no jaundice, dark urine or hematuria were noted.

His past history was negative. Family history—significant only that his mother had nervous stomach and maternal uncle died of duodenal ulcer.

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point is stressed because jejunohepatic adhesions are frequently the cause of postoperative obstruction following gastric resection.

Postoperatively the double lumen metal fitting is equipped with short rubber connections and the suction lumen is handled precisely as an ordinary stomach suction tube irrigating every two hours with tap water and applying constant suction. The feeding lumen is clamped until ten hours postoperatively at which time a liquid high protein digest, fortified with carbohydrate, iron, liver and vitamins, is introduced by gravity flow. Initial feedings of 30 cc every two hours may be gradually increased every twelve to twenty four hours, depending on the clinical picture. In a period of two or three days an optimum protein intake of 100 Gm/day is achieved which can be checked by frequent serum protein determinations. An intake of 1,200 to 1,500 calories daily is also supplied by this type of feeding.

High protein, high calorie digest are prepared for tube feedings by the hospital dietitians and are made available in the quantity desired each day. Formulae for such aliment are available from various commercial houses.

This method of intestinal feeding despite the usual postoperative ileus, provides nourishment by way of the most physiologic route and also provides a small bolus of food which may stimulate the bowel to regain its tone more rapidly.

Parenteral fluid is administered concomitantly to maintain fluid balance and caloric requirements. Oral liquid feedings in small amounts are usually instituted the first day postoperatively and gradually increased. When a positive balance exists between oral intake and suction drainage the Wangensteen suction is discontinued and dependent on a positive balance with gravity drainage the tube can finally be removed. This usually occurs about five days postoperatively. Once the suction-feeding tube is removed it is of no value to replace it and if distention occurs following its removal the tube should be used.

The suction feeding tube can be used for gastroenterostomies as well as gastric resections. It causes no more discomfort than a Levine tube, it is cleaned and sterilized in the same manner as a Miller-Abbott tube and the same tube may be used repeatedly.

#### SUMMARY

1. A simplified suction feeding tube devised for the case of postoperative gastric resections, has been found clinically effective.

A description of the tube, the method of intubation, and postoperative management is presented.

A gastrointestinal ray examination ten days after operation revealed pouch arising at the esophagogastric junction and rising through the esophageal hiatus, the gastric rugae being traced into this pouch. The radiologist made the diagnosis of postoperative diaphragmatic hernia. The diaphragmatic cup was still defective but there was no longer a crater (Fig. 1).

The patient revealed upon questioning that he occasionally regurgitated small amounts of food but that this was innocuous and caused him no trouble. He had had no return of the heart pain since operation and felt much improved. He was discharged on Oct. 30, 1947 and follow-up study was made in the outpatient department. On his first return visit two weeks after discharge the complaint was unchanged. He regurgitated occasional small amounts of undigested food, without apparent correlation to the consistency but considered of no consequence.

#### DISCUSSION

The technique of vagotomy followed in this clinic is that described by Dragstedt and co-workers, who stated: "When satisfied that the vagotomy is complete and that hemostasis has been secured, the operator closes the opening into the mediastinum with three or four catgut sutures. Prior to the case reported here suture of the mediastinal opening had not been routinely performed by us, partly because it seemed unnecessary and partly because of the difficulty in exposing the esophageal hiatus in individuals with deep dimensions in the anteroposterior axis of the upper abdomen. Stimulated by this complication, reconsideration of the problem makes it seem advisable wherever possible to close the esophageal hiatus with silk sutures. It is readily understood how paraesophageal herniation may occur by relaxation of the hiatus due to spreading of the longitudinal fibers of the diaphragm in the delivery of the lower esophagus. The closure may be accomplished without difficulty in the majority of the cases."

#### CONCLUSION

A case of subdiaphragmatic hernia following a hiatus hernia of the paraesophageal type is presented.

#### APPENDIX

Since submission of this report for publication, the patient has been admitted and has undergone repair of the hernia performed on May 24, 1949. When seen one month later he had no symptoms referable to either diaphragmatic hernia or ulcer.

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Physical examination showed blood pressure 173/90; temperature 37° C, pulse 74 respirations, 20. The patient was well nourished and well developed, in no apparent distress, complaining of epigastric pain. Physical findings were limited to the abdomen where there was tenderness to palpation deep in the epigastrium.

Laboratory examination revealed urinalysis negative; blood hemoglobin 15.5 Gm red blood cell 3.6 million; white blood cell 7,000; differential normal. Mucosa negative; blood urea nitrogen 12; blood sugar 104; serum proteins 7. On three stool examination showed guaiac negative; gastric analysis revealed fasting free acid 31 units, aft. histamine 83, 59 and 56 units of free acid at ten minute intervals; gastric analysis after 50 units of regular insulin showed rise to 46 units of free acid; night secretion (8 A.M. to 8 P.M.) 125 cc with 13 units free acid.



Fig. 1—Roentgenogram of stomach and lower esophagus following vagotomy demonstrating gastroesophageal hernia.

Roentgen examination of the gastrointestinal tract revealed an acute duodenal ulcer, the duodenal cap being deformed. There was ulcer crater to its base. Findings from the chest roentgenogram, gall bladder series, and barium enema are negative.

On Oct. 11, 1947, subdiaphragmatic vagotomy was performed through left rectus abdominis under cyclopropane-oxygen anesthesia. An acute duodenal ulcer, almost evidence of obstruction was found. The true gastric ligament of the left lobe of the liver was divided.

Short transverse incision made in the peritoneum over the esophageal hiatus, and the lower esophagus delivered. Two large trunks of the vagus nerve were found and approximately 4 cm. of the posterior agus and 7 cm. of the left were removed. Several small fibers are divided. The esophagus allowed to fall into place and the left lobe of the liver as replaced. The abdomen closed in layers.

The patient's postoperative course was unremarkable. He was placed on gastric suction for six days following operation, at which time the diet was slowly advanced. About seven days postoperative night secretion was 250 cc and there was no free acid following the injection of insulin.

although Beaver and Mann have pointed out that simple irrigation with hypotonic solutions is highly destructive to mesothelium. One must recognize that an open thoracotomy will expose most of the visceral and parietal pleura on one side while even extensive laparotomy will subject only a fraction of the peritoneum to the drying effects of air. When partial or total pulmonary resection is done a generous share of pleura is removed with the specimen and a large dead space remains to upset thoracic physiology and the spatial relationships of the thoracic viscera. Surgical dead space refers to an area which remains after surgical intervention, is isolated enclosed by tissue, and contains only air and other gases. Enormous tumors may be removed from the abdomen without disturbing intra-abdominal pressures but the rigid thorax prevents rapid readjustment which is afforded by the flexible walls of the abdomen.

Clinical experience in World War II has emphasized the importance of prompt removal of blood, fluid and gas from the injured pleural space and rapid re-expansion of the lung which is simply application of the ancient surgical principle that dead space must be eliminated. The modern operation of pneumonectomy requires airtight closure of the thorax and simple readjustment of the intrathoracic subatmospheric pressure which favors full expansion of the remaining lung. Pleural effusion will collect and will eliminate the dead space; this effusion is rarely aspirated unless infection supervenes or an external collection is embarrassing the remaining lung.

The incidence of empyema following simple thoracotomy operations on the heart, the great esophagus, or segmental pulmonary resection or lobectomy is surprisingly low compared to the appearance of this complication after pneumonectomy. Bronchiectasis, a lung abscess, or tuberculosis is such a common infection for pulmonary resection today and there is no doubt that a contaminated field is left in their wake.

Histophysiological methods have been applied to the study of the surface membranes of both peritoneum and pleura for many years. Montoye<sup>1</sup> paid particular attention to the embryology of the elastic layers and Haas and Latarjet and Francillon<sup>2</sup> investigated their relationship and distribution. Mill<sup>3,4,5</sup> described the lymphatic relationships in the visceral pleura. Polleard and Gil<sup>6</sup> studied the entire histologic structure of the various pleural regions in detail. Von Recklinghausen<sup>7</sup>, Maximow<sup>8</sup>, Kampmeier<sup>9</sup> and Mixer<sup>10</sup> selected the milk spot for special study and Noel<sup>11</sup> reviewed and revised the conceptions of structure and function of these mesothelial layers.

Pleural fluid in contact with various irritants has been widely investigated. Its cytologic content and reactions closely resemble those in peritoneal fluid. Borrel<sup>12</sup> showed a consistent sequence of polymorphonuclear leucocytes, followed by mononuclear phagocyte infiltration in such exudates. Opler<sup>13</sup> pointed out that the polymorphonuclear leucocytes contained enzymes which were active only within definite limits of hydrogen ion concentration, but Rouss<sup>14</sup> concluded that the interior of the cell and its enzymatic activity were not influenced by hydrogen ion concentration of the external medium. Kempner

# THE ROLE OF PLEURAL EXUDATION IN INFECTION FOLLOWING PNEUMONECTOMY

## AN EXPERIMENTAL STUDY

JOHN T. SMALL, M.D. AND GEORGE M. HOOKS, Ph.D.†  
ROCHESTER, MINN.

ALTHOUGH there are no important structural differences between the pleura and the peritoneum, the pleura is usually regarded as having ineffective natural resistance to bacterial invasion. The rapid advances of abdominal surgery since the time of Lister developed an early understanding of the normal protective mechanism within the peritoneum. The use of the Fowler position was based on the mistaken belief that the pelvic peritoneum had greater bactericidal powers than that of the upper part of the abdomen. This was the beginning of the trend away from irrigation and free drainage of the contaminated peritoneal cavity which we now know can handle gross soiling under an airtight closure. Even today there is no good evidence that any form of local chemotherapy will add to the natural powers of peritoneal protection except to afford a ready means of drug absorption into the circulation. Within the past decade, as the problems of anesthesia have been solved and our knowledge of thoracic physiology has advanced, intrathoracic surgery has become commonplace, but the ancient fear of pleural weakness is still widespread.

Much of this suspicion of the pleura may be traced directly to the writings of Robinson and Sauerbruch and of Carrel,<sup>2</sup> around the turn of the century. The prominence of these men gave weight to their opinions although neither offered experimental evidence to support his claims. Sauerbruch attempted to show that the pleural surfaces were much less resistant to bacteria than muscle, fat, or the other components of the thoracic wall but Noetzel<sup>4</sup> had refuted such claim in his well-controlled but practically unnoticed work. Carrel had an enviable record in experimental vascular surgery in the thorax and maintained a very low rate of infection in his animals in a day when empyema was the usual sequel to thoracotomy. He protected the exposed pleura with oiled silk and practiced a meticulous technique which was no doubt the major factor in his successes. He maintained that the pleura was peculiarly susceptible to infection or trauma.

## PREVIOUS STUDIES

A review of the many studies of pleural fusion produced by various means and the pleural response to infection and gener-  
ally to infection

Abstractions of thesis submitted by Dr. Small to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M.D. in Surgery.

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gamma globulin fraction, could restrain antibody production. Many have shown that postoperative hypoproteinemia may be due to anesthesia, fasting, trauma, or loss of exudate and that it often accompanies minor surgical procedures.<sup>20</sup> It has not been suggested that a temporary depression of total serum protein may be the beneficial expression of the adequate inflammatory response as blood cells, antibodies, and serum, all rich in protein, are drawn into the involved region. Adams, Thornton, and Thomas<sup>21,22</sup> have reviewed the causes of large loss of blood and of protein in thoracic operations and have attempted to prevent them by placing homogenous plasma in the pleural space after pulmonary resection in order to discourage the formation of the large amounts of exudates which invariably form at the expense of the patient's protein stores.

#### PURPOSE OF STUDY

The purpose of our study was manifold. We proposed to study the nature and origin of the pleural exudate which enters the pleural space after the removal of a lung and to contrast it with exudates which have been produced artificially by foreign irritant. We wished to study the peripheral blood, during the time the exudate was entering the space and to study the cytologic correlation which may exist between the blood and the pleural fluid. We planned to study the histologic changes in the pleural membranes during the time when the exudate was forming. The addition to the pleural space of various substances, such as plasma, dextran, or gelatin foam in order to obliterate the so-called dead space was studied.

Emphasis was given in this study to the immediate postoperative period, wherein infection was most likely to occur and when the exudate was rapidly accumulating. Observations have been made on animals up to one year after pneumonectomy but these data are not included.

#### METHODS AND MATERIALS

Adult fat rats, weighing 250 to 300 Gm and free from any obvious disease, were used for this study. Half albino and half brown dogs were also used for comparison. The data resulted from our detailed study of the changes in the rat form the basis for this report although there were no important differences in the other tissues of these two species.

Prior to pneumonectomy, samples of heart blood were obtained from each rat. From this sample the total erythrocyte and leukocyte count, the hemoglobin level, the percentage of cells as determined by the hemocrit, the differential distribution of the leucocytes, and the total plasma protein level were determined. Simultaneous centrifugation of the sample and centrifuging the blood data and the Hingley modified by ret method<sup>23</sup> were used in the pleural protein determinations. Samples of pleural fluid were obtained from a series of normal rats under postoperative conditions and under the abdominal approach and thoracotomy through the diaphragm. In this study sufficient amounts of fluid were obtained to accomplish all of the following: (1) to study the cytologic characteristics of the exudate; (2) to compare the nature of blood from arteries to the thoracic cavity.

While the animal was under postoperative and an anesthetic, anesthesia, and using the method of intratracheal intubation previously described,<sup>24</sup> the left side of the thorax was opened and the entire left lung was surgically removed. Intracaval ligation of the pedicle structures would not be done but main ligatures were employed in the rat. Every attempt was made to preserve viable specimens. The pleural space and drainage were not used. In the rat it is possible to pull the pedicle out of the thoracic cavity for ligation and removal. In

and Pechel<sup>22</sup> demonstrated the tendency of an exudate to assume an acid reaction and Menken<sup>23</sup> concluded that the cytologic picture in inflammation is dependent on the hydrogen ion concentration of the exudate. In 1911 Lippmann and Pleesh<sup>24</sup> caused the disappearance of granulocytes from the circulating blood of experimental animal with injections of thorium X and found that pleural exudates were then free of these polymorphonuclear cells, a fact which indicated the origin of these cells from the circulating blood.

Steinberg and Diet<sup>25, 26</sup> showed that by a transfer of pleural exudates rich in polymorphonuclear leucocytes they could protect animal from an otherwise fatal pleuritis or peritonitis. However supernatant fluid or cell suspensions did not give the same protection to animals as did whole pleural fluid. Linton<sup>27</sup> transferred stimulated omenta to the peritoneum of other animals, which did not then succumb to a usually fatal injection into the pleural space. He concluded that the recipient animals were protected by the mononuclear phagocytes of the transplanted omenta which migrated to the site of reaction in the thorax. Senn<sup>28</sup> had made similar observations on peritoneal reactions in 1888 and Thompson and Pollack<sup>29</sup> recently transplanted the omenta to the pleural space. Enhanced resistance was induced by Steinberg and Martin<sup>30</sup> in various species with graduated doses of heat-killed streptococci, which resulted in an increase of the mononuclear phagocytes in exudates produced later by bacterial irritant. Menken and Warner<sup>31</sup> have shown by a series of experiments that pleural and other exudates contain a leucocytosis-promoting factor which is passively transmissible to other species.

Inflammation is almost universally regarded as a defense mechanism. The cytologic elements, be they polymorphonuclear or mononuclear presumably offer the most inviting explanation for the *modus operandi*. Goodpasture and Anderson,<sup>32</sup> however departed from these rather orthodox views, established by Metchnikoff<sup>33</sup> and concluded that phagocytic cells may actually promote an infection by favoring growth and invasion by bacteria. Pokrovskaya and Makarov<sup>34</sup> concluded that the polymorphonuclear elastinocyte sequence formed a definite pattern for the excretion or absorption of an irritant. Robertson and van Sant<sup>35</sup> have found that both in vitro and in vivo the mononuclear cells of sterile effusions have greater phagocytic power than the polymorphonuclear cells in pneumococcal infections. Webb<sup>36</sup> has also performed passive transfer of phagocytes from rabbit to rabbit and thus was able to protect the host against otherwise fatal infection. Drinker<sup>37</sup> stated that regardless of cell type abnormally large amounts of exudate will dilute the phagocytic cells and thus enhance the ability of bacteria to proliferate. In other words cell rich exudate will give greater protection against contamination than an exudate with fewer cells.

Wound healing tissue repair and disposition of bacteria, the criteria of resistance are doubtless related to nitrogen balance, protein level, vitamin deficiency<sup>38</sup> and other factors, but they are also certainly dependent on the production of the cellular and humoral elements of the inflammatory response. Cannon, Wheeler, Woolridge and Benditt<sup>39</sup> made the important contribution that in surgical infection prolonged hypoprotecemia, by virtue of depressed

gamma globulin fraction, could restrain antibody production. Many have shown that postoperative hypoproteinemia may be due to anesthesia, fasting, trauma or loss of exudate and that it even accompanies minor surgical procedures.<sup>40</sup> It has not been suggested that a temporary depression of total serum protein may be the beneficial expression of the adequate inflammatory response as blood cells, antibodies, and serum all rich in protein, are drawn into the involved region. Adams, Thornton, and Thomas<sup>41</sup> have reviewed the causes of large loss of blood and of protein in thoracic operations and have attempted to prevent them by placing homogenous plasma in the pleural space after pulmonary resection in order to discourage the formation of the large amounts of exudates which invariably form at the expense of the patient's protein stores.

#### PURPOSE OF STUDY

The purpose of our study was manifold. We proposed to study the nature and origin of the pleural exudate which enters the pleural space after the removal of a lung and to contrast it with exudates which have been produced artificially by foreign irritants. We wished to study the peripheral blood during the time the exudate was entering the space and to study the cytologic correlation which must exist between the blood and the pleural fluid. We planned to study the histologic changes in the pleural membranes during the time when the exudate was forming. The addition to the pleural space of various substances, such as plasma, kolan, or gelatin foam in order to obliterate the so-called dead space was studied.

Emphasis was given in this study to the immediate postoperative period, wherein infection was most likely to occur and when the exudate was rapidly accumulating. Observations have been made on an animal up to one year after pneumonectomy but these data are not included.

#### METHODS AND PROCEDURES

Adult white rats weighing 200 to 300 Gm and free from any obvious disease were used for this study. Healthy mongrel dogs were also used for comparison. The data are tabulated from our detailed study of the changes in the rat from the beginning for this report although there were important differences in the observations on these two species.

From the pneumonectomy sample of heart blood was obtained from white rat. From this sample the total erythrocyte and leucocyte count, the hemoglobin level, the percentage of cells as determined by the hemocytometer, the differential distribution of the leucocytes, and the total plasma protein level were determined. In addition, the blood data and the hemocytometer method as used in the plasma protein determinations. Samples of pleural fluid were obtained from a series of normal rats under postoperative anesthesia, using the pleural puncture and thoracic aspiration through the diaphragm. In this series sufficient amount of fluid was obtained to assemble cytologic data which the cytologic characteristics of the exudates could be compared. The nature of blood from dogs and the observations were similar.

While the animals were under pentobarbital sodium anesthesia and under the method of intratracheal anesthesia as previously described, the left side of the thorax was opened and the entire left lung surgically removed. Indwelling ligatures of the pleural membranes and in the dog hot iron ligatures were employed. The rat. Every attempt was made to prevent exudate entry of the pleural cavity, and drainage was maintained. In the rat it was possible to pull the pleura out of the thoracic cavity for ligation and resection. In

as doing. Blood was not liberated into the pleural space. Those animals which received the most solutions in the empty pleural space are reported as volumes of 0.75 per 100 Gm. of body weight, after closure of the thoracotomy incision. In order to favor adequate expansion of the remaining lung, the intrathoracic pressure was adjusted to 2 to 3 cm. of water. When gelatin foam was used to replace the missing lung in the left pleural space small portions of the substitute are mounted and used in amount essentially equivalent to that of the remaining lung. This material as packed into the pleural space after the costal incision had been closed. The remaining lung was then fully expanded by increasing and sustaining the pressure in the endotracheal tube until the thorax had been tightly closed. The entire procedure involving opening and closing the thorax, required about ten minutes. All animals in which any gross soiling of the pleural space had occurred during the operative procedure are not used in the computation of the data.

Animals were killed postoperatively in groups of three to ten in ranging from one hour to seven days. While the animals were under pentobarbital sodium anesthesia, the abdomen was opened and blood samples were obtained from the ear canals. Small samples of abdominal exudate for cell study are obtained directly through the diaphragm, in the

thorax was to prevent relations of the heart and the right lung to the left pleural space were observed. We did not attempt to and the error diaphragmatic

## RESULTS

### 1 Cytologic Characteristics of the Normal Pleural Fluid of the Rat—

Wide variations between species were noted in the total number of cells per cubic centimeter of fluid in the thorax of normal animal. The average of ten rats sampled was 46,700 cells per cubic centimeter while that of dogs was but 4,500 cells per cubic centimeter. When smears of these fluids were studied differentially (Table I, control) the large mononuclear leucocytes, similar to those seen in peritoneal fluids and exudates and known variously as histiocytes, elastinocytes, or macrophages, preponderated. These comprised in normal animals about 86 per cent of all cells. Small and large lymphocytes occurred in small numbers, and neutrophilic leucocytes were rare but eosinophilic leucocytes represented about 9 per cent of all cells present. Occasional plaques of desquamated mesothelial cells appeared in most of the smears of the pleural fluids.

TABLE I. CYTOLOGIC CHARACTERISTICS OF PLEURAL FLUID AFTER PNEUMOTHORAX

TIME AFTER	CELL COUNT MADE PER CUBIC MILLIMETER OF FLUID	NOTE
LARGE MONONUCLEAR		
		14+8
		0
		0
		0
		0
		0

### 2 Cytologic Characteristics of Pleural Exudates After Pneumectomy—

The changing character of the cellular constituent of the exudates, after pneumectomy is shown in Table I. One hour after operation, the total count had dropped from the accepted figure of 46,700 to 12,400 per cubic millimeter of fluid of these approximately one-half (6,000) were neutrophilic granulocytes. Thus, within one hour after removal of the lung 5,800 neutrophilic granulocytes per cubic millimeter of pleural fluid had already entered the thorax. The number of these cells increased rapidly and at twenty-four hours after operation 4,100 neutrophilic granulocytes were tabulated for each cubic centimeter of fluid. As the volume of the exudate had obviously increased, this represented a tremendous collection of cells. The total number of mononuclear leucocytes per cubic millimeter of pleural fluid dropped very rapidly and was very low at one hour and at three hours after operation. The mononuclear leucocytes began to reappear in the exudate at six hours and were greatly increased at twenty-four hours after operation. At seven days, whereas the total count was low, the number of mononuclear leucocytes was now greatly in excess of the total number of neutrophilic granulocytes.

Small round lymphocytes, few in normal pleural fluid, were greatly increased in the exudates after pneumectomy. These cells appear in the pleural space simultaneously with the fluid exudate containing granulocytes common to the blood stream. Presumably they may be precursors of some of the large mononuclear cells which appear in large numbers later. The eosinophilic leucocytes, ordinarily abundant in normal fluid, were very scarce at three hours after pneumectomy. They did not return in significant numbers until twenty-four hours after pneumectomy. Their absence from the fluid in the early period after operation, we believe is due to their relative infrequency in the blood stream, their rapid infiltration later may be due to a proliferation and subsequent release from the bone marrow.

3 Blood Leucocytes and After Pneumectomy—The total lymphocyte and neutrophilic leucocyte counts made on rats at one, three, six, twenty-four, and seventy-two hours, and one week after pneumectomy are shown in Table II. The total leucocyte count dropped 4,300 cells per cubic millimeter of blood at three hours after pneumectomy. A return to the preoperative level was encountered at six hours but a second fall of 5,000 cells per cubic millimeter of blood occurred at twenty-four hours. At seventy-two hours, the

TABLE II. LEUCOCYTIC COUNT OF BLOOD AFTER PNEUMECTOMY

TIME AFTER OPERATION	LYMPHOCYTES	
	NEUTROPHILS	
	PER CUBIC MILLIMETER	PER CUBIC MILLIMETER
1 hour	17,700	11,700
3 hours	10,800 ± 07	11,700
6 hours	9,400 ± 11	11,700
12 hours	11,900 ± 13	11,700
24 hours	13,300 ± 13	11,700
72 hours	17,500 ± 0	11,700



so doing, blood was not liberated into the pleural space. Those animals which received the anoxic solutions in the empty pleural space were injected with volumes of 0.5 c. per 100 Gm. of body weight after closure of the thoracotomy incision. In order to favor adequate expansion of the remaining lung the intrathoracic pressure was adjusted to 3 to 5 cm. of water. When gelatin foam was used to replace the missing lung in the left pleural space, small portions of the subcutis were incised and wedged in, in most cases actually equivalent to that of the removed lung. This material was packed into the pleural space after the costal sutures had been placed. The remaining lung, as then fully expanded by increasing and sustaining the pressure in the endotracheal tube until the thorax had been tightly closed. The entire procedure involving opening and closing the thorax, required about ten minutes. All animals in which any gross soiling of the pleural space had occurred during the operative procedure were not used in the computation of the data.

Animals are killed postoperatively in groups of three to materials ranging from one hour to seven days. While the animals are under pentobarbital sodium anesthesia, the abdomen was opened and blood samples were obtained from the vena cava. Small samples of pleural exudate for cell study are obtained directly through the diaphragm, in the manner employed on the controls. Mice had not undergone pneumonectomy. The thorax was then opened by removing the sternal plate. After the trachea had been ligated to prevent collapse of the right lung the amount of fluid present was noted and spatial relations of the heart and the right lung to the left pleural space were observed. We did not attempt to determine the exact amount of fluid present in all cases. This is difficult and the error in such determinations is great. Turnings were excised from the mediastinal, diaphragmatic and parietal pleurae fixed, and properly stained for histologic study.

## RESULTS

### 1 Cytologic Characteristics of the Normal Pleural Fluid of the Rat—

Wide variations between species were noted in the total number of cells per cubic centimeter of fluid in the thorax of normal animals. The average of ten rats sampled was 48,000 cells per cubic centimeter while that of dogs was but 4,500 cells per cubic centimeter. When smears of these fluids were studied differentially (Table I control) the large mononuclear leucocytes, similar to those seen in peritoneal fluids and exudates and known variously as histiocytes, elastinocytes, or macrophages, preponderated. These comprised in normal animals about 86 per cent of all cells. Small and large lymphocytes occurred in small numbers, and neutrophilic leucocytes were rare but eosinophilic leucocytes represented about 9 per cent of all cells present. Occasional plaques of desquamated mesothelial cell appeared in most of the smears of the pleural fluids.

TABLE I. CYTOLOGIC CHARACTERISTICS OF PLEURAL EXUDATE AFTER PNEUMONECTOMY

TIME AFTER OPERATION	PER CENT TOTAL					WBC COUNT
	LARGE MONONUCLEAR LEUCOCYTES	NEUTROPHILS	LYMPHOCYTES	EOSINOPHILS	PLASMA CELLS	
Control	40 ± 8.5	0.1 ± 0.1	4.5 ± 0.4	0.1 ± 0.1	0.1 ± 0.1	18 ± 0.5
1 hour	0.6 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0
2 hours	0.1 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0
6 hours	4.0 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0
4 hours	1.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0
72 hours	1.7 ± 1.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0
7 days	8.4 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0

*Cytologic Characteristics of Pleural Exudates After Pneumonectomy—*

The changing character of the cellular constituents of the exudates, after pneumonectomy is shown in Table I. One hour after operation, the total count had dropped from the accepted figure of 46,700 to 1,400 per cubic millimeter of fluid of these approximately one half (6,000) were neutrophilic granulocytes. Thus, within one hour after removal of the lung 6,800 neutrophilic granulocytes per cubic millimeter of pleural fluid had already entered the thorax. The number of these cells increased rapidly and at twenty-four hours after operation 4,100 neutrophilic granulocytes were tabulated for each cubic centimeter of fluid. As the volume of the exudate had obviously increased this represented a tremendous collection of cells. The total number of mononuclear leucocytes per cubic millimeter of pleural fluid dropped very rapidly and was very low at one hour and at three hours after operation. The mononuclear leucocytes began to reappear in the exudate at six hours and were greatly increased at twenty-four hours after operation. At seven days, whereas the total count was low the number of mononuclear leucocytes was now greatly in excess of the total number of neutrophilic granulocytes.

Small round lymphocytes, few in normal pleural fluid, were greatly increased in the exudates after pneumonectomy. These cells appear in the pleural space simultaneously with the fluid exudate containing granulocytes common to the blood stream and presumably they may be precursors of some of the large mononuclear cells which appear in large numbers later. The eosinophilic leucocytes, fairly abundant in normal fluid were very scarce at three hours after pneumonectomy. They did not return in significant numbers until twenty-four hours after pneumonectomy. Their absence from the fluid in the early periods after operation, we believe is due to their relative infrequency in the blood stream, their rapid infiltration later may be due to a proliferation and subsequent release from the bone marrow.

*3 Blood Leucocyte Trend After Pneumonectomy—*The total lymphocyte and neutrophilic leucocyte count made on rats at one, three, six, twenty-four and seventy-two hours, and one week after pneumonectomy are shown in Table II. The total leucocyte count dropped 4,300 cells per cubic millimeter of blood at three hours after pneumonectomy. A return to the preoperative level was encountered at six hours but a second fall of 1,000 cells per cubic millimeter of blood occurred at twenty-four hours. At seventy-two hours, the

TABLE II. LEUCOCYTIC DATA OF BLOOD AFTER PNEUMONECTOMY

TIME AFTER OPERATION	LEUCOCYTES			
	NEUTROPHILS		LYMPHOCYTES	
	COUNT		COUNT	
1 hour	157 ± 12			
3 hours	105 ± 07			
6 hours	84 ± 0.1			
24 hours	219 ± 15	61 ± 0.7	19 ± 0.1	89 ± 0.5
72 hours	115 ± 13	96 ± 0	9 ± 0.4	19 ± 0.5
7 days	175 ± 0.9	84 ± 0.5	44 ± 0.7	64 ± 0.9
				40 ± 0.1

so doing, blood was not liberated into the pleural space. Those animals which received the various solutions in the empty pleural space were injected in volumes of 0.25 per 100 Gm. of body weight, after closure of the thoracotomy incision. In order to favor adequate expansion of the remaining lung the intrathoracic pressure was adjusted to 3 to 3 cm. of water. When galatin foam was used to replace the missing lung in the left pleural space, small portions of the substitute were moistened and wedged in amounts essentially equivalent to that of the removed lung. This material was packed into the pleural space after the costal sutures had been placed. The remaining lung was then fully expanded by mechanical and sustaining the pressure in the endotracheal tube until the thorax had been tightly closed. The entire procedure, involving opening and closing the thorax, required about ten minutes. All animals in which any gross seeping of the pleural space had occurred during the operative procedure were not used in the computation of the data.

Animals were killed postoperatively in groups of three at intervals ranging from one hour to seven days. While the animals were under pentobarbital sodium anesthesia, the abdomen was opened. A blood sample was obtained from the vena cava. Small samples of pleural exudate for cell study were obtained directly through the diaphragm, in the manner employed on the controls, which had not undergone pneumothorax. The thorax was then opened by removing the sternal plate. After the trachea had been ligated to prevent collapse of the right lung the amount of fluid present was noted and spatial relations of the heart and the right lung to the left pleural space were observed. We did not attempt to determine the exact amount of fluid present in all cases. This was difficult and the error in such determinations is great. Tissues were excised from the mediastinal, diaphragmatic and parietal pleurae, fixed, and appropriately stained for histologic study.

## RESULTS

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TABLE I. CYTOLOGY

TIME FROM OPERATION	LARGE		
		PROCENT	PERCENT
Control		100	16.6
1 hour		100	0
3 hours		100	0
6 hours		100	0
24 hours		14	0
72 hours		0.1	0
7 days			

peripheral blood and the total number of leucocytes were both at their lowest level.

*4 Erythrocyte Count and Concentration of Hemoglobin After Pneumectomy*—The data assembled on the erythrocyte counts and the hemoglobin levels preoperatively and at intervals varying from one hour to one week after pneumectomy are shown (Table III). Since this operation entails only a slight loss of blood in the rat, it permitted a study of the effects of loss of lung tissue per se on these blood elements. It will be noted from the data assembled that there were no significant changes in count red, either in the total erythrocyte count or in the grams of hemoglobin per 100 c.c. of blood in any of the pneumectomized animals. Although declines in these two categories were apparent at seven days postoperatively, yet the statistical appraisal of the data indicates that the differences encountered cannot be regarded as significant.

TABLE III. ERYTHROCYTE COUNT AND CONCENTRATION OF HEMOGLOBIN AFTER PNEUMECTOMY

TIME AFTER OPERATION	ERYTHROCYTES, MILLION PER CU. MM. OF BLOOD		HEMOGLOBIN, GRAMS PER 100 C.C.	
	BEFORE OPERATION	AFTER OPERATION	BEFORE OPERATION	AFTER OPERATION
1 hour	9.55 ± .1	9.15 ± .0	14.1 ± .1	13.0 ± .0.5
1 hour	9.51 ± .0.1	8.13 ± .0.9	13.5 ± .0	12.0 ± .1.5
3 hours	9.25 ± .0	.00 ± .0	13.7 ± .0.6	14.4 ± .0.6
4 hours	8.11 ± .0	9.90 ± .0.3	14.0 ± .0.6	13.1 ± .0.6
7 <sup>th</sup> hours	9.07 ± .0.1	8.4 ± .0.3	13.5 ± .0.3	12.8 ± .0.9
7 days	9.0 ± .0	9.04 ± .0.7	13.5 ± .0.1	12.7 ± .0.7

*5 Plasma Protein Level After Pneumectomy*—The total protein level in the blood plasma of fifty normal rats on which operation was not performed was found to range from 4.80 to 5.40 Gm. per 100 c.c. The average of the group was 5.3 Gm. and is represented by the zero line in Fig. 1. One hour after the removal of the left lung the level had dropped 1.1 Gm. from the control figure but at three hours the trend was upward and at six hours the averaged determination was only 0.3 Gm. below the accepted control level. Plasma protein levels did not return to the level obtained for normal animals during the postoperative seven-day period. This phase of the study simply prevented the inclusion of dehydrated animals and distortion of total cell count. The phenomenon of hypoproteinemia after major operations is well known.<sup>22</sup>

*6 The Effect of Pleural Gelatin Foam in the Pleural Space After Pneumectomy*—The anatomic relationships in the thorax after removal of the left lung are shown (Fig. 3). The heart and mediastinum had shifted to the left, the ribs had retracted and the right lung had distended, with herniation of the posterior lobe into the left thoracic space. The diaphragm and liver had been retracted somewhat to portray the dead space where the pleural effusion collects. When gelatin foam was placed in the space after removal of the lung, these changes in anatomic relationships were prevented (Fig. 4). Within seventy-two hours after operation, the gelatin foam had assumed the

<sup>22</sup>Gelatin was supplied through courtesy of The U-John Company, Baltimore, Md.

total number of leucocytes had returned again to its preoperative level. It will be noted (Table II) that the total number of lymphocytes dropped abruptly and remained below its preoperative level at each of the intervals recorded. The neutrophilic leucocytes, however, which were significantly above their preoperative level at one and three hours, had reached a peak of 5,000 cell per cubic millimeter of blood above their preoperative levels at six hours. At twenty-four hours, the total number of neutrophils was not

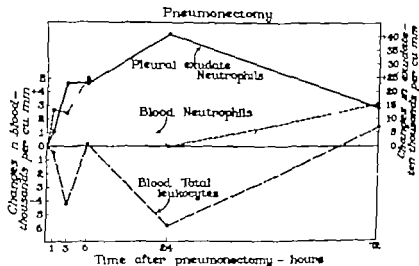


Fig. 1.—The per cent concentration of leucocytes in blood and exudate after pneumonectomy.

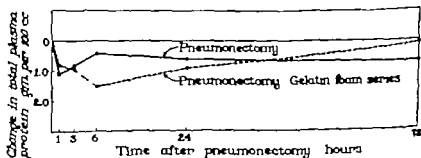


Fig. 2.—Changes in total plasma protein after pneumonectomy.

above the preoperative level but at seventy-two hours, when the postoperative total leucocyte count was again equal to the preoperative count, the number of neutrophils had nearly doubled (Table II). The relationship of the total number of leucocytes and the number of neutrophilic granulocytes in the blood to the neutrophilic component of the pleural exudate at the various intervals is shown (Fig. 1). It will be noted that the neutrophils of the pleural fluid reached their peak at twenty-four hours, at which time the neutrophils of the

TABLE 11. CYTOLOGIC CHANGES IN PLEURAL EXUDATE AFTER PNEUMONECTOMY IN GELATIN FOAM SERIES

TIME AFTER OPERATION	CELLS, THOUSANDS PER CUBIC MILLIMETER				
	MONONUCLEAR LEUCOCYTES	NEUTROPHILS	EOSINOPHILES	LYMPHOCYTES	PLASMS
Control	40 $\pm$ 6.5	0.01	4.7.07	0.4.01	16 $\pm$ 0.2
1 hour	02 $\pm$ 0.1	0.4.01	0.1.01	16.06	0
2 hours	13.0	171.0	0.9.01	15 $\pm$ 0.4	0
4 hours	9.0.10	79 $\pm$ 3.1	0.0.01	03 $\pm$ 0.1	0
6 hours	7.9.17	171.2	0.9.01	0.4.01	0
12 hours	6.8 $\pm$ 1	6.4.15	1.3.01	16.06	0
7 days	6 $\pm$ 1.0	4.1.0	0.0.01	0.4 $\pm$ 0.1	0

With the exception of the six hour period, when the total number of cells was greatest in the gelatin foam series of animals, and of the seven day period the number of neutrophilic granulocytes was consistently lower at each interval than the number of these cells in animals which did not receive the gelatin foam. At one hour after operation there were 5,600 neutrophilic granulocytes per cubic millimeter of fluid less in the animals with gelatin foam than in those without it. At three hours after operation, there were 5,900 and at seventy-two hours, 8,200 fewer neutrophilic granulocytes per cubic millimeter of fluid in animals with gelatin foam than in those without it. At the end of one week, neutrophils were more concentrated in the exudate of the animals with gelatin foam packing.

The data assembled on the leucocytes of the circulating blood of animals at the various interval after pneumonectomy and gelatin foam packing are given in Table 1. There were no significant changes in the total blood leucocyte count at any of the postoperative periods recorded. The only significant stimulation occurred at six hours after operation when the total number of neutrophilic granulocytes had increased 6,500 cell per cubic millimeter of blood over their preoperative level. The changes in the total number of leucocytes in the blood, the numbers of neutrophilic granulocytes in the blood and the numbers of neutrophilic granulocytes in the pleural exudates of pneumonectomized animals with and without gelatin foam are shown in Figs. 1 and 5.

The data assembled from the calculation of the erythrocytes and from the hemoglobin determinations of the pneumonectomized animals with gelatin

TABLE 1. LEUCOCYTES OF THE BLOOD AFTER PNEUMONECTOMY IN GELATIN FOAM SERIES

TIME AFTER OPERATION	LEUCOCYTES, THOUSANDS PER CUBIC MILLIMETER OF BLOOD			
	MYELOCYTES		NEUTROPHILIC LEUCOCYTES	
	BEFORE OPERATION	AFTER OPERATION	BEFORE OPERATION	AFTER OPERATION
1 hour	141.11	101 $\pm$ 1.2		
2 hours	3.07	54 $\pm$ 0.7	4.04	41.6
4 hours	1.0.14	51.04	9.0	54 $\pm$ 0.7
6 hours	7.05	65 $\pm$ 0.6	16 $\pm$ 0.6	101 $\pm$ 1.2
12 hours	1.3 $\pm$ 1.4	9.0.06	41 $\pm$ 0.7	54.06
7 days	1.1 $\pm$ 0.4	12.7.17	4.03	19 $\pm$ 0.9
			29.06	34 $\pm$ 0.2

configuration of the missing lung. The mediastinal shift to the left was prevented, and the so-called dead space in the base of the left hemithorax had been largely obliterated. Effusion was present in animals packed with gelatin foam but in amounts far less than those recovered from pneumonectomized animal without this material. In animals without the gelatin foam an average of 1 c.c. of effusion was recovered from the left pleural space twenty-four hours after pneumonectomy while in those packed loosely with gelatin foam an average of but 0.2 c.c. was recovered. This amount is only slightly in excess of that recovered from the pleural space of animals that did not undergo operation. It is obvious that such data cannot be exact but they do represent trends and indicate that less fluid accumulates when dead space is diminished.



Fig. 3



Fig. 4

Fig. 3.—Necrotic changes in thorax of rat eight days after left pneumonectomy.

Fig. 4.—Anatomic changes in thorax of rat seventy-two hours after pneumonectomy. The left hemithorax had been packed with gelatin foam.

The differential distribution of the cells of the exudate which developed in the thoracic cavity of the animals in which the dead space was packed with gelatin foam after pneumonectomy is shown in Table IV. A comparison of Table IV and Table I shows that, except at six hours, the total number of cells per cubic millimeter of fluid was less in the exudate of animal packed with gelatin foam than in that of animals which were not packed after pneumonectomy. In pneumonectomized animals receiving gelatin foam the largest number of cells (73,000 per cubic millimeter of fluid) was obtained in the exudate six hours after operation. In the series without packing, however, the total number of cells per cubic millimeter of fluid was greatest at twenty-four hours after operation when 73,000 per cubic millimeter were recorded for the exudate.

TABLE IV. CYTOLOGIC CHARACTERISTICS OF PLEURAL EXUDATE AFTER PNEUMONECTOMY IN GELATIN FOAM SERIES

		CYTES, THOUSANDS PER CUBIC MILLIMETER				EXUDATE			
TIME AFTER OPERATION	LARGE MONONUCLEAR LEUCOCYTES		NEUTROPHILS	EOSINOPHILS	YM NOC TES	E NOPHILS			
Control	4	6.5	4.01	4.5±0.7	0.4±0.1	10.0±0.4			
1 hour		0.3±0.1	0.4	0.1	0.1±0.1	1.0	0		
2 hours		1.3±0	1.7	0	0.9	0.1	1.3±0.4		
4 hours		4.6	1.0	7.9	2.1	0	0.1	0.7±0.1	
6 hours		4	1.7	1.7	1	0.0±0.1	0.4	0.1	
72 hours		6.4	1.7	6.4	1.3	1.3±0.1	1.0	0.0	
7 days		0	1.0	4	1.0	0	0.1	0.4	0.1

With the exception of the six-hour period, when the total number of cells was greatest in the gelatin foam series of animals, and of the seven day period the number of neutrophilic granulocytes was consistently lower at each interval than the number of these cells in animals which did not receive the gelatin foam. At one hour after operation there were 5,600 neutrophilic granulocytes per cubic millimeter of fluid less in the animals with gelatin foam than in those without it. At three hours after operation, there were 5,900 and at seventy-two hours, 8,200 fewer neutrophilic granulocytes per cubic millimeter of fluid in animals with gelatin foam than in those without it. At the end of one week, neutrophils were more concentrated in the exudate of the animals with gelatin foam packing.

The data assembled on the leucocytes of the circulating blood of animals at the various intervals after pneumonectomy and gelatin foam packing are given in Table V. There were no significant changes in the total blood leucocyte counts at any of the postoperative periods recorded. The only significant stimulation occurred at six hours after operation when the total number of neutrophilic granulocytes had increased 6,500 cells per cubic millimeter of blood over their preoperative level. The changes in the total number of leucocytes in the blood, the numbers of neutrophilic granulocytes, in the blood, and the numbers of neutrophilic granulocytes in the pleural exudates of pneumonectomized animals with and without gelatin foam are shown in Figs. 1 and 5.

The data assembled from the tabulation of the erythrocytes and from the hemoglobin determinations of the pneumonectomized animals with gelatin

TABLE V. LEUCOCYTE DATA OF THE BLOOD AFTER PNEUMONECTOMY IN GELATIN FOAM SERIES

TIME AFTER OPERATION	LEUCOCYTES, THOUS. PER CUB. MILLIMETER OF BLOOD			
	LYMPHOCYTES		NEUTROPHILIC LEUCOCYTES	
	BEFORE OPERATION	AFTER OPERATION	BEFORE OPERATION	AFTER OPERATION
1 hour	14.1±1.1	13.1±1.1	4.4±0.4	4.1±0.4
2 hours	15.0	15.0±0.7	9	5.4
6 hours	16.0±1.4	22.5±0.8	3.0	0.0
4 hours	7	0.3	4.1±0.1	5.1±0.0
6 hours	1.5	1.4	4.0±0.3	3.9±0.3
7 days	12.1±0.4	12.7	1.7	3.0±0.0
				3.4



foam are given in Table VI. It is obvious that there were no significant changes in the levels of erythrocytes during the seven-day postoperative period. A significant elevation above the preoperative control level in the hemoglobin concentration was recorded at the six hour interval but since this increase was not observed at the later test periods, it presumably represents some artefact and is not accepted as true.

*7 Influence of Various Intrapleural Drugs and Solutions*—Homogenous plasma, solution of acacia (6 per cent) gelatin, and drolan were placed in the pleural space of several series of animals which had undergone the same surgical procedure of left pneumonectomy. These materials were selected as blood substitutes which were in common clinical use and were employed in this study in an attempt to inhibit or to prevent the effusion and the protein depletion which were shown to occur after pneumonectomy. The principal result, however, was an increase of morbidity and mortality rates in each series of

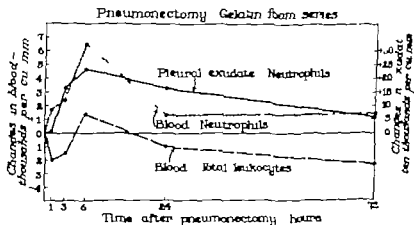


Fig. 3—Change of concentration of leucocytes in blood and exudate after pneumonectomy; the left hemithorax had been packed with gelatin foam.

animals so prepared. Hypoproteinemia was not prevented and the plasma protein levels followed the curve established for the pneumonectomized animals (Fig. 2). The total numbers of leucocytes which appeared in the pleural effusion were extremely inconstant and were at a low level for twenty-four hours. Eight of the group of thirty-two animals were dead within seventy-two hours as a result of empyema. Of the remaining twenty-four six gave microscopic and gross evidence of infection when killed. Studies showed that these animals could tolerate approximately 0.5 cc per 100 Gm of rat of a substitute fluid placed in the pleural space but soon is in excess of this caused either immediate and fatal collapse of the remaining lung or complete cardiac arrest.

In addition to the isotonic blood substitute tested, similar amounts of an amino acid mixture (amigen), 5 per cent ultrathin solution, penicillin (5,000 units per cubic centimeter of isotonic saline solution) and streptomycin (3,000 units per cubic centimeter) were employed. In each of the eight animals

TABLE VI. ERYTHROCYTE COUNT AND CONCENTRATION OF HEMOGLOBIN AFTER PNEUMONECTOMY IN GREY GUinea PIGS

TIME AFTER OPERATION	Erythrocytes MILLION PER CU MM OF BLOOD		HEMOGLOBIN GR PER 100 C OF BLOOD	
	BEFORE OPERATION	AFTER OPERATION	BEFORE OPERATION	AFTER OPERATION
1 hour	853 ± 0.1	851 ± 0	13.7 ± 0.5	13.5 0
2 hours	844 0	841 0.1	11.7 0.0	11.6 0.4
6 hours	836 0	830 ± 0.1	11.4 0.1	11.4 0.1
4 hours	841 1	840 0	14.5 ± 0.4	15 0.9
7 hours	840 0.1	840 0.1	13.6 0.4	13.4 0.5
7 1/2 hr	843 0.3	850 0	14.1 0.4	17.6 0.4

given the amino acid mixture a massive reaction developed with effusion which was almost devoid of any cellular element. Two animals died with empyema and two with a collapse of the opposite lung. The remaining four showed the characteristic hypoproteinemia with all clinical effects. In three of nine animals treated with sulfathiazole solution, empyema developed and the animals died; the remaining six showed hypoproteinemia but survived. No deaths or complications resulted in each group of eight animals given streptomycin or penicillin in the concentration indicated. In comparison with these data a control series of animals which were pneumonectomized but not given substitution therapy all survived. Likewise those in which the dead space was eliminated by means of the gelatin foam packing all survived.

*Reaction After Thoracotomy and Pneumothorax*—Ten animals underwent thoracotomy without pulmonary resection. These were killed at various periods thereafter. It was permitted to remain on the side on which operation was performed with partial collapse of the lung. In each instance there had developed a small pleural effusion exactly similar in cytologic character to that which appeared after pulmonary resection. In all cases there developed a mild hypoproteinemia which persisted for seventy-two hours but there were no significant changes in the leukocytes or the erythrocytes of the circulating blood.

*Reaction of Pleural Membrane After Pneumectomy*—Histologic study of the various pleural membranes revealed marked variations in the extent of the reactions. The first change observed was capillary dilatation in the submesothelial layers as early as twenty minutes after closure of the thorax. After one hour when an effusion was invariably present there was marked edema of the submesothelial layers, persistent capillary dilatation, and extrusion of erythrocytes and leukocytes through the pleural membranes. Mesothelial plaques separated from the pleural surfaces and there was noticeable swelling of the individual mesothelial cells. In the costal pleura the elastic layer, the endothoracic fascia, apparently acted as limiting membrane isolating the underlying lung intercostal muscles, for there were no changes in these deeper structures. In the diaphragmatic and mediastinal pleurae these last layers were less developed so that reactions involving the muscular layers of the diaphragm included edema and a separation of muscle fibers. At seventy-two hours after pneumectomy marked edema of the mesothelium of the mediastinal pleura

was present. This was particularly true in those regions containing fat or lymphatic tissues. Reactions within the pericardial membranes extended into the cardiac muscle where edema and a separation of muscle fiber had occurred. These changes were not observed in any of the pleural or pericardial membranes on the side of the remaining lung.

Fig. 6.



12

Fig. 6—Gelatin foam packing (dark) medial pleura of rat covering heart node placed in heart after pneumothorax.

Fig. 7—Gelatin foam packing from left hemithorax of rat seven hours after pneumothorax (X125).

In the series of animals which had received the gelatin foam after pneumonectomy marked cellular reactions developed in the mediastinal pleura where the gelatin mass had become intimately fused with it. Vascular capillaries extended from the pleura into the gelatin mass, and there was a marked proliferation and migration of fibroblasts into the gelatin. There were no cellular connections, however, between the gelatin mass and the parietocostal pleural membranes. The close connection of the gelatin mass to the mediastinal pleura of a rat twenty-two hours after operation in a region of adipose tissue which over-rides a lymph node is shown in Fig. 6. A higher magnification ( $\times 125$ ) of the same region (Fig. 7) shows the gelatin mass which apparently functioned as a matrix for the extension of fibroblast and capillaries from the mediastinal pleura. The cellular elements at the interface are largely mononuclear phagocytes and young fibroblasts.

#### COMMENT

Pulmonary resection, without surgical collapse of the thoracic wall, as in thoracoplasty, produces a large surgical dead space, a condition which would not be encountered in the abdomen with its collapsible wall. The immediate and sustained reaction of the organism to pneumonectomy is obliteration of this space by a combination of factors which include (1) the overdistention of the remaining lung tissue, (2) the retraction of the parietes, and (3) the production of a fluid exudate. The later effects of pneumonectomy in lower animals cannot be compared to those in man since the patulous mediastinum in the former permits a gradual and complete expansion of the remaining lung which eventually fills the space. However, the early phenomenon of exudation is similar in both low animals and man and appears presumably as a universal expression of irritation or a changed environment for the mammalian pleural membrane.

Packing the pleural cavity after removal of the lung with an inert nondistensible material such as gelatin foam serves to restore the remaining parietal pleura to a more nearly normal pressure status. Under such conditions the effusion which normally occurs after pneumonectomy is greatly inhibited but not completely suppressed and the cellular response in both pleural membranes as well as the exudate is but expression of a mild inflammatory reaction. On the other hand, the extirpation of the exudates and the histologic change of the pleural membranes which ensue on pneumonectomy without gelatin foam packing indicate an extremely high degree of irritation in the pleura. These pleural reactions appear to be comparable to changes which accompany bacterial or other forms of inflammation. The exudate produced in pneumonectomy was invariably present at time of appearance and the histological microscopic and gross changes were always consistent and predictable. The closure of the thorax, followed by the resorption of the intrathoracic pressure to a constant level in pneumonectomized animals, has assured a set of regular conditions for the involved pleura, an adjustment which cannot be attained in clinical investigation owing to the varying ages and varying

was present. This was particularly true in those regions containing fat or lymphatic tissues. Reactions within the pericardial membranes extended into the cardiac muscle where edema and a separation of muscle fibers had occurred. These changes were not observed in any of the pleural or pericardial membranes on the side of the remaining lung.

Fig. 6



Fig. 7

Fig. 6.—Galatin foam packing packed to mediastinal pleura of rat, eosin and fast green (48 hours after pneumothorax) (X125).  
 Fig. 7.—Galatin foam packing from left hemithorax of rat, eosin and fast green (48 hours after pneumothorax) (X125).

cells and serum of the exudate accumulating in the pleural space. Such hypoproteinemias have not been shown to be inconsistent with satisfactory healing in the otherwise healthy animal but it would seem rational to correct a too greatly prolonged hypoproteinemia in the debilitated human being. The placing of isotonic solutions such as plasma, certain blood substitutes, or various drugs in the pleural space after pneumonectomy will not dilute the lower plasma protein level. Furthermore these solutions invariably contributed to a dilution of the cellular elements which are required to combat contamination and to facilitate the repair process.

There was no depletion of the total number of erythrocytes or of the hemoglobin level up to seventy-two hours after pneumonectomy provided the animal was healthy and came to operation with a normal quota of these blood elements. At the later periods, however, we have observed significant declines in these measurements, which persisted for as long as six months.

Normal pleural fluid contains large numbers of cells which are recognized as the totipotent components of the so-called reticulo-endothelial system the function of which is so largely related to reparative processes. This may presumably explain the known clinical and experimental facts which show conclusively that the intact pleural membranes without pneumothorax are capable of resisting heavy assault. The high levels of leucocytes which exist within these normal fluids place them far from the conventional category of a mere thin film of lymph which acts as a lubricant. If we are to regard the total leucocyte level in the circulating blood as an indication of the ability of the organism to combat or respond to an infection, then the enormous number of such cells within normal pleural fluid is certainly not without significance. Earlier studies<sup>22</sup> on the peritoneal fluid of albino rats have shown that a leucocyte level is maintained there which compares very well with the large number of such cells found in the pleural fluids. Furthermore, studies on the differential distributions have shown that the cellular components within the two fluids have almost an exact ratio to one another. The total leucocyte levels in the peritoneal and pleural fluids of the various species appear to be quite parallel to the known natural resistance which these common laboratory animals have attained. The rat is notoriously resistant to an infection of the thorax or abdomen and its almost complete resistance to the tubercle bacillus<sup>23</sup> is a most arresting fact when we compare the leucocyte count of its pleural fluid with that of the more susceptible dog.

The consistent character of the postpneumonectomy exudates under the controlled conditions of the experimental procedures, was correlated with the histologic responses in the various pleural regions. The left diaphragmatic and the lower costal pleurae were found to be irritated in a manner similar to the partial pleura until such time as the effusion developed and apparently protected these structures from the irritating influences of the oscillating pressures exerted by the respirations of the remaining lung.

The most marked and progressive changes were observed in the mediastinal pleura. In each animal in which the inert packing of gelatin foam had been inserted in the pleural space for more than forty-eight hours there was a

pathologic states of the subject. The pleural irritation which follows pneumonectomy appears to be on a purely mechanical basis and is not modified by buffering capacity of tissue, the pH, lymphatic blocking, or concentration of electrolytes. These are variables which need to be considered when various irritants are placed in the pleural space after operation.

The classic theory<sup>14</sup> for the origin of a pleural effusion is not applicable to the effusion which follows pneumonectomy for these older studies eliminate the role of the parietal pleura and consider only the visceral pleura of dead animals *in vitro*. We were unable to find either gross or microscopic evidence that the visceral pleura of the remaining lung had taken part in the production of these pleural effusions. Graham's use of the concept of a changing negative pressure around the visceral pleura serves to emphasize the common misconception that such a negative pressure in some manner is essential to the performance of respiration, in which act it becomes still more negative. In simple emphasis.

In the newborn mammal the lungs completely fill the pleural space, are almost lacking in elastic tissue, and do not collapse to any extent when the thorax is opened.

Small amount of exudate were observed regularly when a simple pneumothorax was done and the cytologic picture of the resulting exudate resembled that found after pneumonectomy. The differences were only quantitative and were further expressed by the changes in total leucocyte level of the circulating blood. When the exudate was relatively large in amount the large number of blood leucocytes which appeared in the exudate were coincident with a drop in total number of blood leucocytes. This relationship substantiates the earlier work of Lippmann and Plech<sup>22</sup> who found no granulocytic cells in the exudates which formed from the irritated pleura of animals whose circulating granulocytes had been destroyed with thorium X and indirectly show the source of these cells from the circulating blood.

The granulocytic infiltration into the pleura thus represents the early phase of the pleural reaction to pneumonectomy. This phase is soon followed by the appearance in the exudate of large numbers of mononuclear leucocytes. This sequence of neutrophilic polymorphonuclear leucocytes, followed by an infiltration of mononuclear phagocytes, is the classic picture of the successful response to any inflammatory condition be it bacterial or chemical. These data do not sustain the view that either the macrophage or the macrophage is the essential element in an inflammatory response but do establish the fact that the pleural response to injury is essentially similar to that observed in the reputedly more resistant peritoneum. The introduction of irritating substances into the pleural space has been shown to produce exudates which are large in volume but low in their cellular contents. The presence of inflammatory cells has been shown by passive transfer experiment to be essential for the destruction of bacteria and we have observed that exudates, low in cellular content, are invariably associated with a marked percentage of mortality and morbidity.

The hypoproteinemias which follow anesthesia and a surgical trauma was marked after pneumonectomy. No doubt this was partly due to the fact that the supply of circulating protein was tapped in order to provide for the

8 The inflammatory response of the pleura is comparable to that of the peritoneum when this protective mechanism is not grossly disturbed

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definite fibrinous attachment of the mass to the mediastinal pleura. This attachment was not observed on the costal or diaphragmatic surfaces until much later. At forty-eight hours, the fibrin content of the exudate as seen in smears, had definitely increased, although quantitative estimations of fibrin were not attempted. The gelatin mass apparently acted as a matrix, for the capillaries and the fibroblasts extended into it from the adjacent mediastinum after eight days. Clotted fibrin was detected histologically in the interstices of the gelatin foam. A dense layer of clotted fibrin accumulated along the costal pleura forty-eight hours after pneumonectomy. Fibroblasts and capillaries extended eventually into the gelatin mass but this action was far less marked than from the mediastinum and the firm fibrous attachment of the gelatin to the costal pleura did not occur until much later.

Experimental observations indicate that the mediastinum is the site at which exudates largely appear and are removed from the pleural space. In this sense therefore the mediastinum serves the pleural space much as the omentum serves the peritoneal space.

#### CONCLUSIONS

The following conclusions have been reached in this study:

1. Small amounts of pleural fluid may be obtained from the pleural spaces of laboratory animal. Cytologically this fluid is rich in mononuclear leucocytes and the concentration of these cells appears to bear some definite relationship to the natural resistance known to occur in certain species.

2. A pleural effusion invariably occurs after pneumonectomy. This effusion is the apparent result of an irritation of the diaphragmatic, mediastinal, and costal pleural membranes, melted by the changes in pressure exerted by the respiratory movements.

3. The cytologic patterns of these pleural exudates are definite and resemble those which obtain in any inflammatory reaction. The initial response is an infiltration of polymorphonuclear leucocytes in such tremendous numbers as to induce a simultaneous leucopenia and to indicate cell origin from blood stream reserves. The secondary response includes the infiltration of mononuclear phagocytes derived largely from adjacent tissues but partly also from the blood lymphocytes.

4. The dilution of effusions with either plasma, blood substitutes, or irritating drug solutions is accompanied by increased morbidity and mortality rates in these experimental animal. Moderate concentrations of penicillin and streptomycin in the pleural spaces do not disturb the cell content of exudates or unfavorably affect the mortality rate.

5. The amount of the pleural effusion after pneumonectomy may be greatly reduced by the elimination of the so-called dead space with an inert packing of gelatin foam.

6. The mediastinal pleura is comparable in certain functions to the greater omentum of the peritoneum.

7. An early post-operative decrease of erythrocytes and hemoglobin is due to loss of blood at operation and not to loss of pulmonary tissue per se.

## THE EFFECT OF STREPTOMYCIN LOCAL AND SYSTEMIC ON CONTAMINATED SUTURED WOUNDS

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SINCE the time of Hippocrates surgeons have tried to reduce mortality and improve the healing of contaminated and infected wounds by the local application of a wide variety of substances. Recognition that most agents which kill bacteria also injure tissues finally led in the 1920's and 1930's to the virtual abandonment of wound antiseptics. Interest in local wound applications revived with the discovery of the sulfonamides. Being strongly bacteriostatic with slight if any toxic effect on tissues, much was expected of them and at the beginning of World War II enthusiasm for the local use of sulfonamides was great. In carefully controlled studies of civilian wounds, however, and in the extensive experience of military surgeons, sulfonamides applied locally were found to contribute little to the problem of wound infection. Near the end of the war their use was discontinued by the United States Army. The ineffectiveness of sulfonamides used locally is probably due to inhibition of their action in blood, pus, and tissue fluid, and to the relative resistance to their action of common wound contaminants, particularly the staphylococcus and gram-negative bacilli.

The local use of penicillin in wound management has also been disappointing because of its narrow range of antibacterial activity, its transient effect, destruction of its activity by changes in pH, and inactivation by the products of many bacteria commonly found in wounds. Although effective at times when repeatedly instilled in joint and pleural cavities containing susceptible organisms, local application to open and sutured wounds has been of little value.

Streptomycin with few limitations than the sulfonamides and penicillin appears, in theory at least, to be a more suitable agent for application to wounds. It has a wide antibacterial range being effective against both gram-positive and gram-negative organisms, and against many organisms which are resistant to the sulfonamides and to penicillin. It acts rapidly in the presence of blood and pus and is relatively nontoxic to tissues. Streptomycin has been used in conjunction with Sulfamylon in the local treatment of experimental and clinical wounds by Howes, who believes that Sulfamylon may be more effective than streptomycin because of its wide antibacterial range and a great resistance to changes in pH. There has been no report to our knowledge of the local use of streptomycin alone under controlled conditions.

In the experiment herein reported sutured wounds produced in a standardized manner have been inoculated with a standard dose of gram-positive and gram-negative organisms, a method resulting in 100 per cent wound infection.

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**Streptomycin**—For local application to the wounds an ointment base was used as a vehicle the composition of the base being carbowax (100 Gm.) and polyethylene glycol (1.0 cc). Streptomycin was added to make a concentration of 5,000 units per cubic centimeter. Ten cubic centimeters of the ointment, containing 50,000 units of streptomycin were applied to each wound with a spatula, special care being taken to prevent leakage of the broth culture and ointment.

In the animals treated systemically 2,000 units of streptomycin per kilogram were injected intramuscularly every six hours for six days.

**Experiments**—Four groups of animals were studied as follows:

**Group A—Control** The wound were inoculated with the organisms and closed. No streptomycin was used (twenty-two animals).

**Group B**—The wound were inoculated with the organisms and closed. No local streptomycin was used. Beginning two hours after the operation, streptomycin, 2,000 units per kilogram, was injected intramuscularly every six hours for six days (nine animals).

**Group C**—Streptomycin, 50,000 units in the ointment base was applied to the inoculated wound before closure (twenty animals).

**Group D**—The inoculated wounds were loosely closed to prevent leakage of the broth culture and sterile dressings were applied. Eight hours later the wounds were reopened. Streptomycin, 50,000 units in the ointment base was applied, and the wounds were closed with tight sutures, as in the other groups (ten animals).

The wounds were dressed and inspected every three days. On the sixth postoperative day blood cultures were taken, skin sutures were removed, and if there was any drainage wound cultures were taken. Toxicity was noted.

Animals which died were autopsied. There was seldom any question whether death was due to anesthesia, distemper or wound infection with septicemia. In case of doubt death was ascribed to wound infection.

## RESULTS

The results of the experiments are summarized in Table I. Animals which died as the result of anesthesia or distemper are not included in this analysis. In Table II the blood cultures and wound cultures are tabulated.

In Group A, the controls, all of the wound became infected and had positive cultures. In all it could be considered mild, while in the others there were remarkably virulent undermining wound infections with extensive necrosis of the skin and subcutaneous tissue in most instances. In those where it did not occur for several weeks. Most of the animals were profoundly toxic showing little interest in their surroundings or in food. Thirty-eight per cent had positive blood cultures. In all death was clearly due to anesthesia or distemper and in nine (63 per cent) of the remaining animals death was attributable to infection.

\*The possible antibacterial effect of the ointment base per se was determined by the local application of the base (without streptomycin) to inoculated wounds in dogs. The degree of infection and the clinical course in these animals were similar to the controls.

and 53 per cent mortality in control animals. The efficacy of streptomycin in controlling the infection has been investigated by (1) systemic (intramuscular) administration of streptomycin after inoculation with the organisms, (2) local application of streptomycin at the time of inoculation with the organisms, and (3) local application of streptomycin eight hours after inoculation with the organisms.

#### EXPERIMENTAL METHOD

**The Wound**—Wounds in dogs are notably resistant to infection and a survey of the literature did not disclose a reliable experimental method of producing wound infection. The method of William White simulating traumatic wounds which become infected in human beings, has proved effective.

**Operation**—The hair on the dog's back was clipped and shaved from the inferior angle of the scapula to just below the iliac crest and the dog was anesthetized with intravenous sodium pentobarbital†. After preparation of the skin with iodine and alcohol, an incision 6.0 cm. long was made 2.0 cm. lateral to the pincus process, beginning just below the last right rib. The muscle fascia was incised, and the incision was carried down into the underlying muscle to a depth of 1.0 cm. Silk ligatures were used for hemostasis. Six large Kocher clamps, 7½ inches in length, were applied to the muscle on one side of the wound, taking bites at least 0.5 cm. deep, and three of these were ligated with silk. The three remaining Kocher clamps were removed after ten minutes. The same procedure was repeated on the muscle on the other side of the wound and on the subcutaneous tissue on both sides of the wound. One cubic centimeter of the broth culture of organisms was then introduced into the wound with a pipette, care being taken to prevent leakage, and the wound was closed. Five interrupted silk sutures were placed in the muscle and fascia and five vertical mattress sutures in the skin, all sutures being tied as tightly as possible without breaking the No. 00 silk. The wounds were covered with sterile gauze dressings secured with 1-inch adhesive strips wound completely around the dog's body.

**The Organisms**—In order to produce wound infections similar to those in human beings, recent reports concerning the bacteriological flora of infected wound were studied. The commonest wound pathogens appear to be the staphylococcus, streptococcus, and the colon bacillus, and these were chosen. Equal amounts of twenty-four broth cultures of *Staphylococcus aureus*, *Streptococcus hemolyticus* and *Escherichia coli* were mixed in a test tube and 10 c.c. of the mixture was transferred to a 100 c.c. bottle. The turbidity of the mixture was such that 23,000,000 streptococci, and 23,000,000 staphylococci, and 23,000,000 *E. coli* were present. The sensitivity of the organisms was 91 µg. *S. aureus* 13.0 unit per cubic centimeter, *S. hemolyticus* 0.33 unit per cubic centimeter, and *E. coli* 10 unit per cubic centimeter.

† Properly associated with the Harrison Disinfectant of Parke, Davis & Co. (Chicago, Ill.)  
 (Veterinary pentobarbital (pentobarbital Na) Abbott Laboratories, Chicago, Ill.) each cubic centimeter of this preparation contains 1.0 gr. of pentobarbital the dosage used was 0.1 cc. per kilogram.

sight drainage on the tenth postoperative day but healing was complete by the fourteenth day. Streptomycin blood levels in four of the animals six hours after an intramuscular injection of streptomycin were 4.0, 4.0, 3.0 and 2.0 units, respectively.

In Group C local application of 50,000 units of streptomycin in the ointment base at the time of inoculation with the organisms modified the infection to about the same degree as intramuscular administration in Group B. Most of the animal appeared unaffected by the organisms, and in all but two the wound were healed on the tenth postoperative day. Two had positive blood cultures, and one which died, had a severe wound infection with marked toxicity and skin necrosis. In several the wounds were fluctuant without sign of inflammation on the sixth postoperative day and when the sutures were removed, the ointment was extruded. Coaptation of the wound surfaces following extrusion of the ointment resulted in rapid healing. In only two were the wound cultures positive.

In Group D local application of the streptomycin at a second operation eight hours after inoculation of the wounds with the organisms, did not appear to be less effective than simultaneous application in Group C. The two groups are not large enough for statistical comparison. When the wounds were reopened, the tissues had lost their normal glistening appearance and were slightly edematous. One animal had a severe wound infection with a positive blood culture and died. Extrusion of the ointment when the sutures were removed was also noted in this group. In only two was there a positive wound culture; however, all but two of the wounds were healed on the tenth postoperative day.

#### CONCLUSIONS

These experiments were designed to test the effect of streptomycin on contaminated sutured wounds and to compare the effectiveness of local and systemic administration of streptomycin in preventing virulent wound infection. Although the number of animals studied is not large, streptomycin appeared effective in controlling both local and invasive infection.

A significant modification of the virulent infection of control animals by the prophylactic systemic administration of streptomycin was expected since the organisms were streptomycin-sensitive. A single local application of 50,000 units of streptomycin in an ointment base appeared to be as effective as intermittent intramuscular administration for six days. This was true both when the streptomycin was applied locally at the time of inoculation with the organisms and when applied eight hours later after multiplication and invasion of the bacteria had begun.

A single local application of streptomycin in these experiments apparently inhibited the streptomycin-sensitive organisms for a sufficient period of time to prevent serious infection in most instances, and this occurred in the presence of necrotic tissue. The different groups of animals studied are not large enough for statistical comparison.

The occurrence of streptomycin-resistant organisms in many human traumatic wounds would be expected to limit the clinical effectiveness of strepto-

TABLE I ANALYSIS OF EXPERIMENTAL DATA

CRITERIA OF LOCAL AND SYSTEMIC INFECTION	GROUP	GROUP	GROUP	GROUP
	CONTROLS (%)	STREPTOMYCIN 25,000 U. PER KG M. EVERY 6 HR FOR 6 D (%)	STREPTOMYCIN 50,000 U. A TIME OF OPERATION (%)	STREPTOMYCIN 50,000 U. LOCALLY 8 HOURS AFTER IN OPERATION (%)
Death due to local and invasive infection	53	0	14	0
Toxicity on 6th post operative day	69	13	14	14
Purulent wound drainage on 6th post operative day	100	37	14	75
Profuse	89	0	7	8
Slight	13	37	7	21
Wounds with extensive skin necrosis and severe underlying infection	65	0	7	14
Positive blood culture on 6th postoperative day	75	0	7	14
Positive wound culture on 6th postoperative day	100	37	14	25
Complete wound healing on 10th postoperative day	8	75	86	25

In Group B the prophylactic intramuscular administration of streptomycin resulted in a greatly altered postoperative course. In contrast to the toxic, lethargic animals in Group A (controls) most of these dogs were alert and active and ate well. There were no deaths due to infection and no serious infections. There were no positive blood cultures. In almost one-third there was slight purulent drainage when the sutures were removed on the sixth postoperative day but signs of inflammation in these wounds were minimal. There was still

TABLE II ANALYSIS OF BLOOD AND WOUND CULTURES

GROUP	BLOOD CULTURES				WOUND CULTURES			
	POSITIVE (%)	STAPH COCCI (%)	ENTERIC COCCI (%)	OTHER COCCI (%)	POSITIVE (%)	STAPH COCCI (%)	ENTERIC COCCI (%)	OTHER COCCI (%)
A Controls	37	81	50	37	100	81	75	81
B Streptomycin 25,000 U. per kg I.M. every 6 hr for 6 days	0				37	100	80	100
C Streptomycin 50,000 U. locally at time of operation	7		16		14	100	75	100
D Streptomycin 50,000 U. locally 8 hr after operation	0				86	100	25	0

slight drainage on the tenth postoperative day but healing was complete by the fourteenth day. Streptomycin blood level in four of the animal six hours after an intramuscular injection of streptomycin were 40, 40, 30 and 90 units, respectively.

In Group C local application of 50,000 units of streptomycin in the ointment base at the time of inoculation with the organisms modified the infection to about the same degree as intramuscular administration in Group B. Most of the animals appeared unaffected by the organisms, and in all but two the wound were healed on the tenth postoperative day. Two had positive blood cultures, and one which died had a severe wound infection with marked toxicity and skin necrosis. In several the wound were fluctuant without signs of inflammation on the sixth postoperative day and when the sutures were removed, the ointment was extruded. Coaptation of the wound surfaces following extrusion of the ointment resulted in rapid healing. In only two were the wound cultures positive.

In Group D local application of the streptomycin at a second operation eight hours after inoculation of the wounds with the organisms, did not appear to be less effective than simultaneous application in Group C. The two groups are not large enough for statistical comparison. When the wounds were reopened, the tissues had lost the normal glistening appearance and were slightly edematous. One animal had a severe wound infection with a positive blood culture and died. Extrusion of the ointment when the sutures were removed was also noted in this group. In only two was there a positive wound culture however and all but two of the wounds were healed on the tenth postoperative day.

#### CONCLUSIONS

These experiments were designed to test the effect of streptomycin on contaminated, sutured wounds and to compare the effectiveness of local and systemic administration of streptomycin in preventing virulent wound infection. Although the number of animals studied is not large streptomycin appeared effective in controlling both local and invasive infection.

A significant modification of the virulent infection of control animals by the prophylactic systemic administration of streptomycin was expected since the organisms were streptomycin-sensitive. A single local application of 50,000 unit of streptomycin in an ointment base appeared to be as effective as intermittent intramuscular administration for six days. This was true both when the streptomycin was applied locally at the time of inoculation with the organisms and when applied eight hours later after multiplication and invasion of the bacteria had begun.

A single local application of streptomycin in these experiments apparently inhibited the streptomycin-sensitive organisms for a sufficient period of time to prevent serious infection in most instances, and this occurred in the presence of necrotic tissue. The different groups of animals studied are not large enough for statistical comparison.

The occurrence of streptomycin-resistant organisms in many human traumatic wounds would be expected to limit the clinical effectiveness of strepto-



TABLE I ANALYSIS OF EXPERIMENTAL DATA

CRITERIA OF LOCAL SYSTEMIC INFECTION	GROUP A	GROUP B	GROUP C	GROUP D
	CONTROLS (%)	STREPTOMYCIN 25,000 U PER KG IM EVERY 6 HR FOR 6 DA (%)	STREPTOMYCIN 50,000 U IM OF OPERATION (%)	STREPTOMYCIN 50,000 U. SCAL 8 HOURS AFTER OPERATION (%)
Death due to local and systemic infection	57	0	14	0
Toxicity on 6th post- operative day	68	1	14	14
Purulent wound drain- age on 6th post- operative day	100	37	14	29
Prefero	99	0	7	9
Alight	12	3	7	29
Wounds with extensive skin necrosis and severe undermining infection	63	0	7	14
Positive blood culture on 6th postoperative day	25	0	7	14
Positive wound culture on 6th postoperative day	100	3	14	29
Complete wound healing on 10th postoperative day	8	75	86	82

In Group B the prophylactic intramuscular administration of streptomycin resulted in a greatly altered postoperative course. In contrast to the toxic lethargic animals in Group A (controls) most of these dogs were alert and active and ate well. There were no deaths due to infection and no serious infections. There were no positive blood cultures. In almost one-third there was slight purulent drainage when the sutures were removed on the sixth postoperative day but signs of inflammation in these wounds were minimal. There was still

TABLE II ANALYSIS OF BLOOD AND WOUND CULTURES

GROUP	BLOOD CULTURES				WOUND CULTURES			
	POSITIVE (%)	STAPHYLOCOCCI (%)	TRYPANOCYTES (%)	WOUNDS (%)	POSITIVE (%)	STAPHYLOCOCCI (%)	TRYPANOCYTES (%)	WOUNDS (%)
A. Controls	29	86	50	73	100	93	75	87
B. Streptomycin, 25,000 u. per kg. IM. every 6 hr for 6 day	0				37	100	50	100
C. Streptomycin, 50,000 locally 1 time of operation	7		16		14	100	75	100
D. Streptomycin, 50,000 locally 8 hr after incision	0				29	100	29	

## A METHOD FOR PUNCTURING BLOOD VESSELS LOCATED AND EXPOSED BY INCISION

HENRI MICHEL LAMM, M.D., LA FAYETTE, TEXAS

INFUSIONS or transfusions may become difficult and pressing problems when a vein can be neither seen nor felt because of obesity or general circulatory collapse. A recently described method of infusing into the femoral vessels which uses the pulse of the femoral artery as a guide (Shaffer) can be used only if this pulse can be felt. In an obese patient or in a patient in circulatory collapse this pulse often is impalpable. In such an emergency but two ways remain: bone marrow infusion or infusion into a vessel located by surgical exposure—cutting down on the vein.

If surgical exposure is chosen, one may either transect the vessel and insert a cannula rigid or semirigid or an infusion catheter of soft rubber (Lamm) or one may choose needle puncture. Either method has its advantages and disadvantages. Cannulation permits fluid administration over a comparatively long time while needle administration usually is limited to hours. On the other hand, cannulation invariably leads to the eventual destruction of the vessel used while needle administration usually preserves its patency. Cannulation is often technically difficult, while needle puncture should be easy especially with the method to be described.

The principle of any good needle puncture of a vessel is that the angle between needle axis and vessel axis must be very acute.

An approach at a right angle between needle and vessel involves the following pitfalls: (1) The needle may push the vessel away rather than enter it; (2) If it does penetrate one wall of the vessel it very easily may also penetrate the other wall; (3) The bevel may be longer than the inner diameter of the vessel and thus may lie only partly within its lumen; (4) Slightest movements of patient or operator may dislodge the needle. All of these dangers are reduced to a minimum if the needle pierces the vessel at a very acute angle.

If the incision exposing the vessel were parallel to it the desirable very acute angle approach would be easy. Usually, however, one cannot use an incision parallel to the vessel as one does not know its exact location, especially in just those cases where the need is most urgent that is, when the patient is in collapse or is obese. In these patients, where it can be neither seen nor felt one will use an incision from first to the course of the vessel (of which one has usually a good idea although the vessel's exact location is not known). If one tries to puncture a vessel through such an incision, it will be approached at almost a right angle especially if it lies deep as in the obese patient. All the pitfalls enumerated here will be risked, that is, lateral displacement, transverse sticking-out of part of bevel and easy dislodging.



## A METHOD FOR PUNCTURING BLOOD VESSELS, LOCATED AND EXPOSED BY INCISION

HENRICH LAMM, M.D., LA FOLIA, TEXAS

**I**NFUSIONS or transfusions may become difficult and pressing problems when veins can be neither seen nor felt because of obesity or general circulatory collapse. A recently described method of infusing into the femoral vessels which uses the pulse of the femoral artery as a guide (Shaffer<sup>1</sup>) can be used only if this pulse can be felt in an obese patient or in a patient in circulatory collapse, this pulse often is unpalpable. In such an emergency but two ways remain: bone marrow infusion or infusion into a vessel located by surgical exposure—cutting down on the vein.

If surgical exposure is chosen, one may either transect the vessel and insert a cannula, rigid or semirigid, or an infusion catheter of soft rubber (Lam<sup>2</sup>) or one may choose needle puncture. Either method has its advantages and disadvantages. Cannulation permits fluid administration over a comparatively long time while needle administration usually is limited to hours. On the other hand, cannulation invariably leads to the eventual destruction of the vessel used, while needle administration usually preserves its patency. Cannulation is often technically difficult while needle puncture should be easy especially with the method to be described.

The principle of an "good" needle puncture of a vessel is that the angle between needle axis and vessel axis must be very acute.

An approach at a right angle between needle and vessel involves the following pitfalls: (1) The needle may push the vessel away rather than enter it. (2) If it does penetrate, no wall of the vessel is very easily may also penetrate the other wall. (3) The bevel may be longer than the inner diameter of the vessel and thus may be only partly within its lumen. (4) Slightest movement of patient or operator may dislodge the needle. All of these dangers are reduced to a minimum if the needle approaches the vessel at a very acute angle.

If the incision exposing the vessel is parallel to it the desirable very acute angle as previously would be easy. Usually, however, one cannot use an incision parallel to the vessel, as one does not know its exact location, especially in just those cases where the needle is most urgent; that is, when the patient is in collapse or obese. In these patients, where veins can be neither seen nor felt, one will use an incision from the site of the course of the vessel (of which one has usually a good idea although the vessel's exact location is not known). If one tries to puncture a vessel through such an incision, it will be approached at almost a right angle especially if it lies deep as in the obese patient. All the pitfalls enumerated here will be risked, that is, lateral displacement, transfixion, sticking-out of part of bevel and easy lodging.

The advantage of the transverse incision, that is the ease with which it permits one to locate a vessel can however be combined with the advantages of the very acute angle approach.

A short segment of the vessel is exposed by transverse skin incision and blunt dissection of the subcutaneous fat. The infusion needle is then inserted *through the skin* a certain distance away from the incision (about three or four times the thickness of all tissue overlying the vessel) just over the presumed course of the vessel such skin puncture being distal from the incision; puncturing a vein, and proximal when injecting into an artery. Then the needle point is advanced *subcutaneously* toward the exposed segment of the vessel, until it appears just over it in the depth of the wound. The vessel is punctured *under the guidance of the eye* advancing the needle until all of its bevel rests well within the lumen.

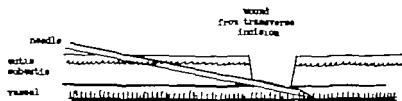


FIG. 1

This method has been found useful in infusions and transfusions. It may also serve well in injecting into arteries, for example, in arteriography and in therapeutic arterial injections, as of penicillin solutions.

#### SUMMARY

Puncture of a vessel located and exposed by an incision transverse to its course can be done reliably and easily by approaching it with a needle which punctures the skin away from the incision and whose point travels subcutaneously until it appears in the depth of a wound over the bare vessel where it punctures it at a very acute angle and under the guidance of the eye.

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## SOME TECHNICAL CONSIDERATIONS IN THE ARTERIOGRAPHIC EXAMINATION OF THE LOWER EXTREMITY

R. GLENN SMITH, M.D. AND DARRITT A. CAMPBELL, M.D. ELOPSE, MICH.

(From the Department of Surgery, Wayne County General Hospital and University of Michigan)

THE arteriographic examination of the lower extremity in various peripheral vascular states is an important addition to other tests now employed.<sup>1</sup> The method is not new, having been performed first upon an amputated extremity eleven weeks after the discovery of the roentgen ray. Since that time it has undergone investigation intermittently, but has never become a popular method of examination. This unpopularity has not been due to the paucity of information obtained, but rather to the cumbersome and difficult method by which the procedure was accomplished. For this study a simple and uncomplicated method was devised. It is the purpose of this report to summarize the more important technical aspects of this procedure which have been gained in our series of over 100 arteriograms.

### CONTRA INDICATIONS

Since this method of examination was used for the first time in living subjects by Seward and Forester, Berberich and Hesch, and Warner and Brooks in 1923 and 1924, many radiopaque agents have been utilized for intra-arterial injection. Most of these substances have fallen into disuse, however, because of undesirable side effects. Pain, for example, has been severe enough with some agents to require general spinal anesthesia. Others have necessitated surgical exposure of the artery to avoid extravascular deposition of the drug which otherwise would have resulted in extensive tissue destruction. Diiodal and thiodal are among those which have survived a long period of trial. For a purpose Diiodal seemed to possess few disadvantages and was used in all cases in connection with 30, 50 or 70 per cent. Kollidion and Stenbom<sup>2</sup> and others<sup>3,4</sup> have studied extensively the occurrence of systemic reactions with the intravenous and intra-arterial administration of this substance. All precautionary measures adopted<sup>5</sup> to determine unusual sensitivity were known in our series, and no reactions were noted.

### GENERAL CONSIDERATION IN THE POST-EXAMINATION ACCOMPLISHMENT OF A SATISFACTORY ARTERIOGRAM

If this method of examination is to be superior to other tests now employed for the purpose of evaluating various types of peripheral vascular states, it must (1) reveal satisfactorily the extent, type and location of pathologic lesion, and (2) be easily interpreted. The interpretation and classification of an arteriogram are contained in another report. In the performance of this method of examination certain characteristic features should be enumerated:

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The advantage of the transverse incision, that is the ease with which it permits one to locate a vessel can however be combined with the advantages of the very acute angle approach.

A short segment of the vessel is exposed by transverse skin incision and blunt dissection of the subcutaneous fat. The infusion needle is then inserted through the skin a certain distance away from the incision (about three or four times the thickness of all tissue overlying the vessel) just over the presumed course of the vessel such skin puncture being distal from the incision in puncturing a vein, and proximal when injecting into an artery. Then the needle point is advanced *subcutaneously* toward the exposed segment of the vessel, until it appears just over it in the depth of the wound. The vessel is punctured under the guidance of the eye advancing the needle until all of its bevel rests well within the lumen.

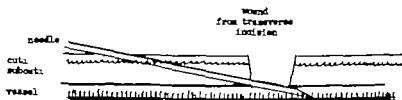


Fig. 1

This method has been found useful in infusions and transfusions. It may also serve well in injecting into arteries, for example in arteriography and in therapeutic arterial injections, as of penicillin solutions.

#### SUMMARY

Puncture of a vessel located and exposed by an incision transverse to its course can be done reliably and easily by approaching it with a needle which punctures the skin away from the incision and whose point travels subcutaneously until it appears in the depth of wound over the bared vessel where it punctures it at a very acute angle and under the guidance of the eye.

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Lamm, Herrick. *Infusocatheter* (Zentralbl. f. Chir. 63: 2078, 1970).

puncture being made under the direction of the palpating finger of the opposite hand, which is guided by the arterial pulsation.

8 If this method of examination were to be employed in many patients and conducted by a limited number of examiners, the question of overexposure should be considered. For the occasional examiner this would be of little significance. But if this factor were felt to constitute a real danger the needle should be connected to the syringe by appropriate rubber tubing and the examiner should remain outside the field during exposure.

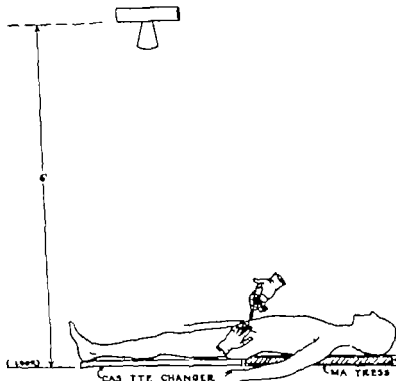


Fig. 1.—The patient is positioned for arteriography lying on mattress on the floor beneath the cassette tunnel. The involved extremity is in place on the specially designed cassette tunnel (Fig. 2). The position on the floor is necessary to obtain exposures at all levels with the ordinary radiographic equipment in which the tube cannot be raised six feet above the table. Exposures of this distal area are needed to visualize the entire arterial tree of the lower extremity after one injection.

9 In order to change the cassettes as rapidly as desired and when desired without disturbing the position of the extremity or the position of the needle in the artery a cassette tunnel (Fig. 2) has been specially constructed. To expose the arterial system of the entire lower extremity the patient is placed on a mattress on the floor at a distance of 4 feet from the tube (Fig. 1).

#### TECHNIQUE

The patient is placed on the mattress and cassette tunnel (Fig. 1) with the cassettes in the proper position in the tunnel (Fig. 2). The area below the



1 Primarily the object of the method is to visualize the functioning lumen of the arterial system of the lower extremity. Small collaterals entering the lower extremity cannot serve as sources of entry for the injection of radiopaque substances, thus, the first requirement is a patent major artery at a point where it enters the extremity. If this requirement is not present, the examination encompasses more than an extremity and as a result becomes more complicated.<sup>12</sup>

2 Arterial disease clinically present in the distal portion of the extremity frequently is a result of pathologic states in the proximal portion of the arterial tree.<sup>13</sup> For this reason, the radiopaque material must be injected at the most proximal part of the extremity and the entire arterial system be included in the examination.

3 The contrast media employed must be in sufficient concentration in the lumen of the artery to give good visualization on a roentgen film. Hawley<sup>14</sup> gave 5 per cent as the minimal intraluminal concentration of thorotest for this purpose and found comparable results with iodine compounds. To obtain this concentration, it is important to use a needle of adequate size and equipment capable of rapid injection of the necessary calculated amount.

4 The mean velocity of the flow of blood in the normal femoral artery has been estimated to be 23 cm per second. Blood flowing at this rate through the artery will sweep the contrast media well before adequate visualization of the artery is obtained unless it is retained. In cases with occlusion of major branches, this rate will be considerably slowed, but it is sure that the velocity in all cases will be decreased. It is necessary to occlude the femoral artery while injecting the opaque media until the film is exposed. This is best accomplished by digital compression of the femoral artery just above the site of injection.

The rate of diffusion of contrast media in arterial branches of equal size is markedly different from one partially or completely occluded. Thus, an open branch may have sufficient media to show a shadow long before the occluded branch. Such evidence recorded on film could be interpreted as occlusion at the bifurcation. To avoid such mistaken ideas, two complete roentgenograms with a short period of time interposed are required at each examination. The need for at least two serial films is further demonstrated in cases with segmental occlusion of major vessels. Blood (and contrast media) is occluded in major vessels below such an occlusion by traversing smaller collaterals, which assist in slowing the rate of flow. In some cases, depending upon the extent of the segmental occlusion and the distance of the filling collaterals, the flow in the proximal artery below the occlusion may actually be retrograde. Thus, the contrast media may be considerably delayed in reaching the distal portion of the leg.

5 To avoid pain at the site of injection and motion of the extremity during exposure it is necessary to anesthetize the skin and internal analgesic procaine hydrochloride.<sup>15</sup>

7 The introduction of the needle through the skin and into the lumen of the femoral artery requires little explanation. A special built-in required, the



1 - For information of



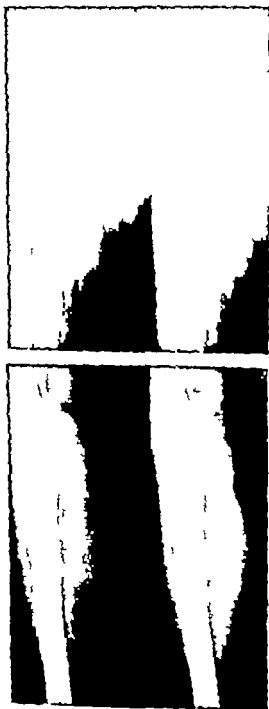


Fig. 2.—Anteropographic of the feet, showing the feet in a normal position. The feet are crossed, the toes pointing towards each other. The feet are not estimated to the left of the feet.

inguinal ligament is prepared with suitable antiseptic and the artery palpated. The site of injection is anesthetized with 1 per cent procaine hydrochloride, infiltrating along both sides and above the artery. Thirty cubic centimeters of 25 per cent Diodrast are aspirated into a 30 c.c. Luer Lock syringe and this is connected to a long 18 gauge short beveled needle. The needle with syringe attached is inserted into the artery under the direction of the palpating finger of the opposite hand. The fingers of the opposite hand are kept in position to occlude the artery above the site of injection which is made about 1 cm. below the inguinal ligament. The artery is compressed against the pubic ramus and the Diodrast injected as rapidly as possible. When 25 c.c. have been injected, the first exposure is made. The tray of the cassette tunnel is pushed to position of second exposure (Fig. 4, E) and the digital pressure on the artery released for four seconds, meanwhile injecting the remaining 5 c.c. of the solution. At the completion of the injection the second exposure is made. The exposures are made at a distance of 1/2 feet, using 68 kv and 300 Ma for 1/20 second.

At the completion of the procedure the patient may become flushed and warm and should be forewarned of momentary pain in the leg during the injection has occurred in some patient.

#### SUMMARY

1. Some important features in the success of performance of arteriography of the lower extremity have been reviewed.

The technique of the method is described.

3. The details of the construction of a simple inexpensive but efficient cassette tunnel for the rapid changing of cassettes during the procedure is presented.

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# THE VALUE DERIVED FROM UTILIZING THE COMPONENT PARTS OF THE TRANSVERSALIS FASCIA AND COOPER'S LIGAMENT IN THE REPAIR OF LARGE INDIRECT AND DIRECT INGUINAL HERNIA

A GROUP OF CASES

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PRIOR to 1939 in all cases of repair of inguinal hernia I employed the Bassini operation or one of its modifications, in which the various deep layers of the inguinal space were sutured to the inguinal ligament. Recurrences resulted at a rate of 5 to 10 per cent in oblique hernia and a higher percentage in direct hernia. The majority of the recurrent cases were within the first year following operation. Seventy-five per cent recurred as direct hernias superior to the pubic tubercle and posterior to the external abdominal ring. The remainder recurred as indirect hernias, doubtless due to failure to remove the hernial sac or to inadequate closure of the internal abdominal ring.

Eight years ago in some cases of large indirect, direct, and recurrent hernias I began to utilize the component part of the transversalis fascia, aponeurosis of the transversus abdominis muscle and Cooper's ligament. For the last five years this type of operation has been employed exclusively in such cases. For the small hernia as seen in children, in cases where the internal abdominal ring is not markedly dilated and the transversalis fascia is not impaired, the removal and closure of the hernial sac and closure of the ring are all that are required.

This study is based on 116 operations for large oblique, recurrent and direct inguinal hernias. There were 68 patients, 18 of whom had bilateral hernias. A questionnaire was sent recently to each of the patients, asking if there had been any recurrence of hernia, and there were replies from all except 3 whose questionnaires were returned as undelivered. In the answered questionnaires, without exception, the patients stated that there had been no recurrence. In only one case was there infection following operation. After the infection cleared up there was no interference with or weakness of the inguinal support.

Ninety-one patients in the series were male and 25 females. There were 13 in the age group up to 10 years, 1 between 20 and 30 years, 16 between 30 and 39 years, 4 from 40 to 49 years, 14 between 50 and 59 years, 11 from 60 to 69 years, 9 in the group 70 to 79 years and 1 patient in the ninth decade of life, both aged 81 years. The youngest patient was born of 13 years. The greatest percentage of cases (44 per cent) occurred in patients between the ages of 40 and 49 due to the fact we believe that this is the period of life when relatively strenuous activity is most likely to precipitate a break or giving way

of the supportive inguinal tissues where there is a congenital weakness of the transversalis fascia.

Forty nine cases involved the right side only 31 the left side only and 18 or 36 per cent were bilateral. Seventy four of the hernias, or 63.6 per cent were oblique and 4 or 36 per cent were direct. There were four strangulated hernias. Five of the patients had had recurrences prior to this

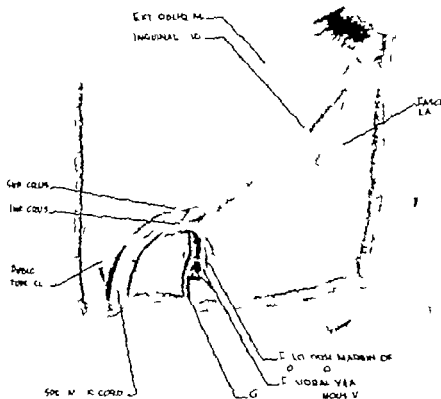


FIG. 1.—Superficial dissection of the deep fascial structures of the inguinal region. Right upper half, fascial and superficial muscles; left, lower half.

time. The average size of the hernial left was 7.8 by 6 cm. The largest defect was 12 by 10 cm. The average length of time in bed was ten to twelve days, as compared with eight to twenty-one days in the Bassini operation. The average length of time before return to work (hard labor) was four to six weeks. Lighter duties were resumed at the end of three weeks.

#### HISTORICAL

In recent years there has been a growing realization among surgeons of the need for fuller knowledge of the anatomy of the transversalis fascia, Cooper's



ligament, and the internal abdominal ring in the repair of hernia. This realization has been widely reflected in the literature.

The surgical utilization of the transversalis fascia and attached structures, including the transversus abdominis aponeurosis, together with Cooper's ligament, in hernial repair is, however, no longer new. In 1914 Testut and Jacob<sup>14</sup>

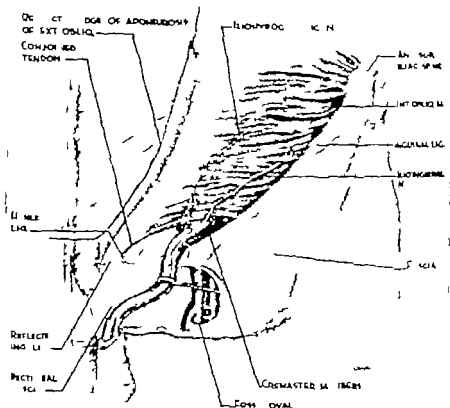


FIG. 3.—Transversalis musculofascial and nerv. structures of the inguinal region.

described in detail the component parts of the transversalis fascia and Cooper's ligament. In 1938 Arnon and Miel<sup>15</sup> found, after a study of 120 cadavers, that the aponeurotic portion of the transversus abdominis muscle showed a marked variation in its position in the inguinal region. In only 3 per cent did the muscular portion extend to the level of the spermatic cord. In 62 per cent it terminated in the superior half of the inguinal region, and in 7 per cent it was not inguinal at all. In approximately 19 per cent the layer was almost as aponeurotic as the external oblique. In the same subject the muscle fibers terminating at or near the interspinous line. Medially also there was considerable variation in the extent of the muscular part of the layer. In only about one-

half the cases did the muscle fibers form the lateral two-thirds of the stratum in the inguinohypogastric area and the aponeurosis the medial one-third, as is consistently the arrangement for the internal oblique. Subsequently (1942) McVay and Anson<sup>11</sup> pointed to the error in the Bassini operation of approximating the transversalis fascia to Boupart's ligament.

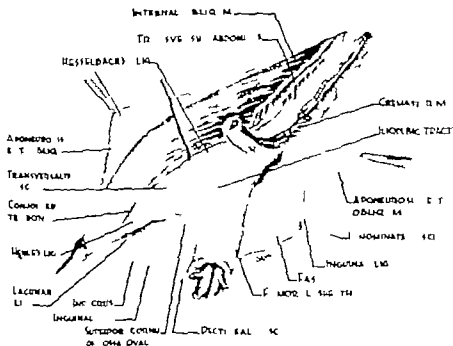


Fig. 3.—The transversalis fascia in the inguinal region. The relationship of the iliopectineal tract, transversalis fascia and the femoral sheath is shown. The inguinal ligament and fascia lata are shown cut and reflected. The transected aponeurotic portion of the external oblique and the nerve branches beneath it are reflected to show the iliopectineal tract of the transversalis fascia. The iliopectineal tract is continuous with the femoral sheath below. The aponeurotic portion of the transversalis fascia is continuous with the transversalis sheath and the iliopectineal tract. The iliopectineal tract is continuous with the transversalis sheath and the iliopectineal tract. The iliopectineal tract is continuous with the transversalis sheath and the iliopectineal tract.

Surgically Lotbomen in 1693 employed Cooper's ligament and the pectineal fascia in the cure of femoral hernia. Not until 1922 when Wise furnished the germ for the idea was the regular Bassini stitch carried by loop on through the inguinal ligament so as to include a portion of the pectineal fascia. On the basis of this idea the following men approximated the lower end of the inguinal fold to the iliopectineal fascia and Cooper's ligament to illustrate the critical angle above the pubic bone: Andrews (1924), Babcock (1927), Dickson (1936), and during the last decade McVay and Anson (1941), Nuloff (1941), Harkins and associates (1942), and most recently Clark and Hashimoto (1946).

In the more common types of inguinal herniorrhaphy such as advocated by Bassini, the medial portion of the transversalis fascia, commonly known as Hesselbach's ligament, and variously the transversus abdominis aponeurosis and the internal oblique muscle are sutured to the inguinal ligament, making a poor substitute for their normal insertion. The inguinal ligament is not the insertion of the transversalis fascia, transversus abdominis muscle and the

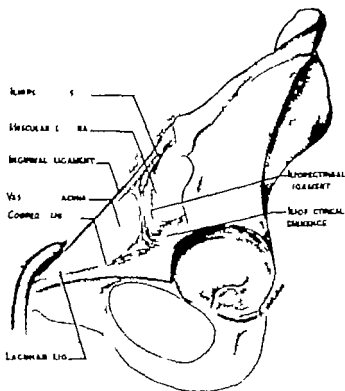


Fig. 4.—This diagram shows the location of Cooper's ligament, attached to the pubic bone inferiorly and to the inguinal ligament superiorly, and its relationship to the transversalis fascia and the inguinal ligament. The weak support of the inguinal ligament is pointed out.

Internal oblique muscle. Its relationship to these structures is merely one of proximity. Anatomically the inguinal ligament is weak in the low inguinal region. The only support it receives is from its insertion to the pubic bone medially, the anterior superior iliac spine laterally, and its attachment below to the fascia lata (Fig. 4). Surgically the inguinal ligament does not provide a suitable substitute for the insertion of these structures (the transversalis fascia, transversus abdominis, and internal oblique muscles) because it is composed of fibrous tissue. In the repair of large indirect recurrent, and direct

hernias, it is recommended that the component parts of the transversalis fascia (Hesselbach's and Hough's ligaments and the iliopectine tract) be united with and anchored to Cooper's ligament, which is formed by the blending of these structures and the pectineal fascia onto the pubic bone. Cooper's ligament is the normal insertion, and, as McVay and Anson (1940) have aptly put it, is readily accessible, intrinsically strong and directly fixed to bone.

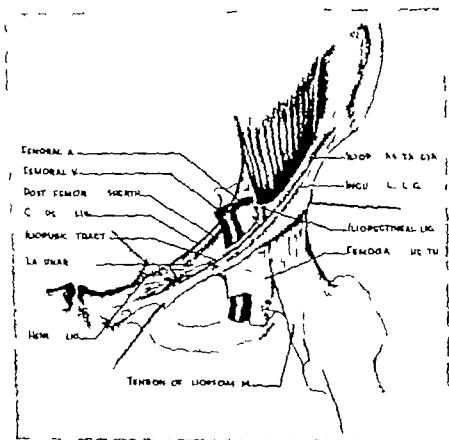


Fig. 1.—Deep body and histomorphologic structure of the inguinal region. This diagram shows the interrelations of Cooper's ligament (the superior pubic ligament) to Hough's ligament, iliopectine tract, the iliopectine tract, the iliopectineal ligament, and the inguinal ligament. The femoral vessels are displaced slightly laterally in order to clarify the structures about the femoral canal.

#### ANATOMY\*

The transversalis fascia is a connective tissue or fascial membrane located between the peritoneum and the transversus abdominis muscle. It furnishes the chief fascial support for the anterior abdominal wall. In the inguinal

\*The author wishes to thank William Robert Hough, M.D., and Katherine M. Hough, M.D., for their assistance in the preparation of this manuscript.

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region the transversalis fascia becomes thick and strong reinforcing unprotected areas. Here the fibers assume a fan shape as they receive support at their different points of insertion. The handle portion occupies the upward position and the lower or open portion fastens onto the pubic bone and the different ligamentous trunks of this area. Along its medial portion it becomes blended with fascia of the rectus muscle and laterally with the deep iliopectineal fascia beneath the inguinal ligament. From the lower inguinal region it projects into the thigh with the femoral vessels as the femoral sheath. In the inguinal region

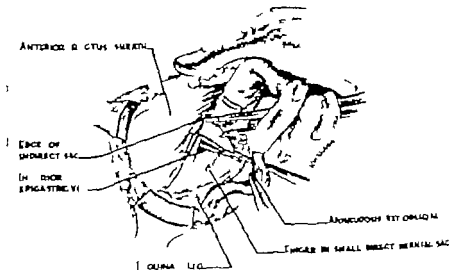


FIG. 3.—Direction of the hernial sac for the diagnosis of direct and femoral hernia. If inserted into the peritoneum, it can be demonstrated by applied to the fundus, traction to become part of direct hernial sheath.

the transversalis fascia is potentially weakened in two areas: the upper or mid portion of the fascia is pierced by the internal abdominal ring and the lower portion, above the pubic bone in the unprotected area commonly called the Hesselbach space does not receive support from the internal oblique and the transversus abdominis muscles. As a result of its modifications in the inguinal region, the following components of the transversalis fascia are derived: the ligament of Hesselbach (ligament interfoveolare), Henle's ligament and the iliopectineal tract.

**Ligament of Hesselbach or the Ligament Interfoveolare.**—The ligament of Hesselbach is located just lateral to the inferior epigastric vessels and along the medial margin of the internal inguinal ring in the inguinal space (Figs. 3 and 4). Its fibers are chiefly vertical and triangular in shape due to its attachment above and fixation below. Externally it receives fibers from the trans-

versus abdominis aponeurosis. It is inserted below at the pecten of the pubes, where its fibers fuse into Cooper's ligament, and in its upper insertion its fibers pass laterally to the internal abdominal ring medially across to the sheath of the rectus muscle and finally extend to the secondary arcuate line which lies below the fold of Douglas.

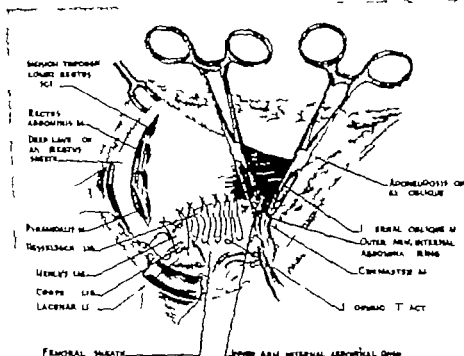


Fig. 7.—First row of sutures. Three sutures are placed 1 to 2 in. apart, through Hesselbach's ligament and iliopectineal ligament above and Cooper's ligament and the lacuna ligament below, including the medial part of the iliopectineal tract. The third suture is the last one, incorporating Cooper's ligament. The remaining sutures, peritoneal, Hesselbach's ligament, the iliopectineal tract up to the level of the internal abdominal ring, come in with Hesselbach's ligament. Here is the level of the aponeurosis of the transversus abdominis muscle as included in the suture bit. In this drawing, vertical relaxing incision has been made in the part of the anterior rectus fascia posterior to the external oblique aponeurosis. The internal ligament is not shown. The 1st row of the internal abdominal ring has been interrupted and brought into view with Allis clamps preparatory to their proximalization. It is interrupted sutures above the spermatic cord.

**Ligament of Henle.**—Henle's ligament lies in the floor of the inguinal space (Figs. 4, 5 and 6). Its fibers run chiefly in the transverse direction. It is somewhat triangular in shape and concave above. Its base is inserted onto the pubic bone. Its outer fibers blend with the iliopectineal fascia, the base of Cooper's ligament, and the base of Hesselbach's ligament. Along its medial surface it receives fibers from the lowermost portion of the rectus fascia.

**The Iliopubic Tract or the Ligament of Thompson.**—The iliopubic tract forms the outer leaf of the transversalis fascia (Figs. 3, 6, and 7). It lies beneath the inguinal ligament. Medially it swings posteriorly and attaches to

region the transversalis fascia becomes thick and strong reinforcing unprotected areas. Here the fibers assume a fan shape as they receive support at their different points of insertion. The handle portion occupies the upward position and the lower or open portion fastens onto the pubic bone and the different ligamentous tissues of this area. Along its medial portion it becomes blended with fascia of the rectus muscle and laterally to the dense iliopectineal fascia beneath the inguinal ligament. From the lower inguinal region it projects into the thigh with the femoral vessels as the femoral sheath. In the inguinal region

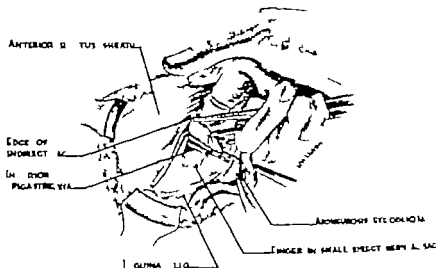


FIGURE 3. Inguinal region of direct and femoral hernia. Anterior ilius sheath, edge of direct AC, in ryon pigastrie vla, ovina lio, acromiomyosculum, finger by small direct hern a sac.

the transversalis fascia is potentially weakened in two areas: the upper or medial portion of the fascia is pierced by the internal abdominal ring and the lower portion above the pubic bone in the unprotected area commonly called the Hesselbach space, does not receive support from the internal oblique and the transversus abdominis muscles. As a result of these weaknesses in the inguinal region, the following components of the transversalis fascia are derived: the ligament of Hesselbach (ligament interfoveolare), Henle's ligament and the iliopectineal tract.

**Ligament of Hesselbach or the Ligament Int of reglare**—The ligament of Hesselbach is located just lateral to the inferior epigastric vessels and along the medial margin of the internal inguinal ring in the inguinal space (Figs 3 and 7). Its fibers are chiefly vertical and it is triangular in shape due to its attachment above and fixation below. Externally it receives fibers from the trans-

middle inguinal fossa and the internal inguinal or supravesicular fossa, and it is through the middle inguinal fossa that the majority of direct inguinal hernias occur. Rarely does the hernia originate in the internal inguinal fossa, which lies medial to the obliterated umbilical artery. Here the transversalis fascia gets support from the rectus sheath and the conjoint tendon. In dealing with a large direct inguinal hernia it is very important after the hernial sac has been dealt with to close the opening in the transversalis fascia through which the hernia made its exit which closure is independent of the support obtained by approximating the different component portions of the transversalis fascia and utilizing Cooper's ligament.

#### ANESTHESIA

Spinal anesthesia is used unless contraindicated when local anesthesia is employed. For the local anesthesia a 1 per cent solution of Novocain and 3 drops of a tetracain chloride to the ounce are employed. The objection to local anesthesia in repair of inguinal hernia is the time consumed in its injection. It usually requires thirty to forty minutes longer. In the inguinal region a complete block anesthesia from local Novocain injection, however, can be obtained with complete relaxation of the tissues with the minimum amount of solution.

The Balfour incision is employed. The incision should not extend onto the scrotum or the low pulse area, as the skin in these areas harbors bacteria and if these tissues are incised it may lead to infection of the wound. In the only two cases of infection in the series, both occurred where incisions had been extended onto these areas. With a blunt retractor placed in the low angle of the wound, sufficient exposure of the deeper structures can be obtained without incising the low pulse or scrotal area. In cases of hernia the superficial vessels of the lower angle of the wound often are larger and more numerous than in the upper angle possibly due to the irritation from the hernial bulge or pressure from a truss. To maintain hemostasis the larger vessels should be carefully ligated out and doubly ligated before they are divided. The smaller vessels and the capillaries should be clamped and ligated. This prevents hematoma and minimizes serum accumulation, thus decreasing the danger of infection and interference with tissue repair.

The suture material is either cotton or silk. A heavy grade is used for the deep sutures medium for the external aponeurosis and Scarpa's fascia and fine for hemostasis. The chief value of nonabsorbable material over surgical suture (catgut) is that it maintains apposition of the tissues until union occurs, and prevents tissue reaction for serum accumulation further reducing the risk of infection.

The skin incision is carried through Scarpa's fascia to the aponeurosis of the external oblique muscle (Fig. 1) where sponge retraction should be employed to keep open the areolar and adipose tissues from the surface of the aponeurosis throughout the incision. The aponeurosis is opened by a small incision in the upper angle of the wound. With elevation of the margins of the aponeurosis, the incision is carried through the fibers down to and including the substance



the pecten of the pubes, in company with the outer leaf of Henle's ligament, the base of Cooper's ligament, and the iliopectineal fascia. Laterally it is attached to the anterior superior iliac spine, where its fibers spread like a fan in a divergent manner some going to the spine itself and others onto the internal lip of the iliac crest. It receives additional support from the femoral sheath and the iliopectineal fascia, which is partially evident as it crosses the femoral vessels. Roughly its fibers are both vertical and transverse. Many of the transverse fibers cross the inguinal space, blending with Hesselbach's ligament, and with the lateral border of the adminiculum lineae albae.

*Cooper's Ligament or the Superior Pubic Ligament*—Cooper's ligament extends from the tubercle of the pubis along its superior border to the iliopectineal eminence (Figs 4, 5 and 7). It is formed by the fusion of the pubic attachments of the three component portions of the transversalis fascia (Hesselbach's ligament, Henle's ligament, and the iliopectineal tract) and the pectineal fascia. It appears as a thick, fibrous cord intimately adherent to the bone and runs posteriorly at an angle of 30 to 35 degrees to the inguinal ligament. Because of its strength and position its utilization in the repair of inguinal hernia is very important.

*The Internal Abdominal Ring*—The internal abdominal ring, as described by Lytle, stands out as the pivot around which the transversalis fascia is arranged, located midway between the anterior superior spine of the ilium and the pubis, approximately 2 cm. above the inguinal ligament (Fig 7). It is made up of sling fibers derived from the transversalis fascia and attached to the undersurface of the transversus abdominis muscle. The ring is not round, but is U-shaped. Its open ends point upward and the angle of the ring points downward. The fibers of the angle of the ring are much shorter than the fibers of either arm. The fibers of the medial arm of the ring are much longer than the fibers of the outer arm, and often the fibers of the medial arm are found attached as far up as the arcuate line or the fold of Douglas. The outer arm fibers, being shorter and smaller find their attachment to the transversus abdominis muscle in proximity to the anterior superior spine of the ilium. The arrangement of the ring fibers gives a freer movement of the internal arm when the abdominal muscles are brought into action by the different exercises of these muscles and produces a somewhat sphincterlike action of the abdominal ring. (For further details of the anatomy and the physiology of the internal abdominal ring, consult Lytle<sup>24</sup>.)

*The Inguinal Space*—The inguinal space, or outer suprpubic space is the space that is not covered by the transversus abdominis and internal oblique muscles (Figs 2 and 3). It is in this space that the transversalis fibers are the weakest and usually its fibers here run transversely. It represents the dome portion of the transversalis fascia, with the weakest support, commonly called Hesselbach's triangle, the base of which is formed by the medial portion of the inguinal ligament the medial side by the lateral border of the rectus abdominis muscle and its lateral border by the inferior epigastric vessels. It is through this space that direct inguinal hernias occur. This space is divided into the

and invite recurrence. Passing the suture through and over the muscles may also interfere with the action of the muscles and weaken them by strangulation.

The complete removal of the hernial sac and closure of the internal abdominal ring are essential for a successful operation for oblique hernia. In the closure of the ring both arm and the angle of the ring should be identified. This can be done by elevating the spermatic cord and freeing adhesions beneath the cord by sponge dissection down to the angle of the ring. The angle of the ring will appear as dense fibers firmly adherent to the bed of the transversalis fascia. From this point each arm of the ring will be seen to run in line with its normal position. To facilitate the exposure of each arm, an Allis clamp may be placed on its fibers, and with elevation of the clamp the respective arms will come into view (Fig. 7). After such exposure the arms of the ring are approximated by two to three interrupted sutures above the cord. In placing the sutures one should avoid incorporating the spermatic cord tissues or closing the ring so tightly as to constrict the cord.

After the hernial sac and the hernial ring have been properly treated it is necessary to clear the inguinal canal of areolar and adipose tissue, accessory vessels, and straggling muscle fibers. Most frequently the accessory vessels are found beneath the cord as it swings over the pubic bone. Often the vessels are of large size and they should be doubly clamped before dividing. In the recurrent herniaarring fibrous bands of tissue will be found adherent to the inguinal ligament from the previous approximation of the apposite structures to the ligament. The inguinal ligament is to be freed of the fibrous tissue. This affords good visualization of the operative field including the component parts of the transversalis fascia and Cooper's ligament. Cooper's ligament may be identified as a fibrous cord by palpation of the superior margin of the pubic bone. It is covered by the thin pectineal fascia, and it can be readily discerned by placing an Allis clamp onto the pectineal fascia so as to include the ligament.

For statistical purposes the size of the hernial cleft may be obtained by a linear and transverse measurement of the cleft using a graduated uterine probe.

Upon examination, the hernial cleft may be found to be of such size that, with retraction of the Howelbach ligament and the aponeurosis of the transversus abdominis muscle approximating these structures to the iliopectineal tract and Cooper's ligament may lead to tension along the suture line. In such cases, Rituchoff and others have suggested incising the rectus fascia at its pubic attachment extending the incision in an upward manner for several centimeters (Fig. 7). This will provide relaxation of these structures for normal tissue closure. It has been found that such a procedure will not weaken the rectus muscle and thus diminish muscle support. However in only one case in this series was a relaxing incision in the rectus fascia found necessary due to atrophy of Howelbach's ligament and the transversus abdominis aponeurosis following a previous operation for hernia.

Closure of the hernial cleft should be begun at the lower angle of the wound over the pubic bone. Harkins and Swenson preferred placing the first suture several centimeters above the pubic bone in proximity to the femoral vein to lessen the chance of injury to the vein in placing a suture. I recommend

ring. The ring is opened along its upper medial surface, bringing the ilioinguinal and iliohypogastric nerves into view (Fig 3). The ilioinguinal nerve runs parallel to and medial with the spermatic cord. Opposite the subcutaneous ring the ilioinguinal nerve divides into several branches, some of which often pierce the ring fibers of the external oblique aponeurosis. Good exposure prevents injury to these nerve fibers when the ring is opened. The iliohypogastric nerve makes its superficial exit several centimeters above the bed of the ilioinguinal. It runs in a transverse direction and pierces the rectus fascia along the outer margin. Injury to either nerve may result in weakening the muscles, which may encourage a recurrence of the hernia. Also, injury to the ilioinguinal nerve and its fibers at the subcutaneous ring will produce a numbness of the scrotum and medial skin surface of the thigh.

The ilioinguinal nerve is further protected by being dissected from its bed and withdrawn in an outward lateral manner. The spermatic cord is separated from its bed of adhesions and is withdrawn in a like manner. In many cases the hernial sac is of such size that it fills the entire canal. It is difficult in such cases to determine whether the hernia began as an oblique or a direct since there is a giving way of the entire transversalis fascial support. The deep epigastric vessels which normally run inferior and medially to the internal abdominal ring no longer serve as a guide for diagnosis between an oblique and a direct hernia. When the hernial bulge attains large size these vessels are sometimes displaced to a position above and opposite the internal abdominal ring. The diagnosis of small direct or femoral hernia suggested by Fallis' constitutes a real advance in the recognition of these hernias when they have not been observed by routine examination. Fallis suggested, in cases of small direct hernia, opening the peritoneum at the internal abdominal ring above and medial to the spermatic cord. The surgeon's finger enters the peritoneal cavity and the entire inguinal space, including the femoral region, is palpated for weak points and peritoneal pouching (Fig 6).

In the management of small direct hernias, or cases where the dome portion of the transversalis fascia is herniated, when they accompany oblique hernias, their treatment should be carried out in the fashion recommended by Hoguet. However, for the large direct hernia with definite sac formation, the Hoguet method is not applicable. This type of hernia is treated in the same way as an oblique hernia. This is accomplished by freeing the hernial sac of adhesions down to the abutment of the peritoneum. In both large direct and oblique hernias, the hernial opening in the peritoneum is closed by purse-string suture placed on the inside of the sac at its base. An alternative for the purse-string suture is the transfixed stitch placed at the base of the open sac. In the large direct hernia, the hernial ring in the transversalis fascia must be closed independently of the reconstruction of the fascia.

The practice of anchoring the stump of the sac to the undersurface of the overlying muscles in the oblique hernia has been advocated by some as the best method of preventing recurrence of hernia. It has been observed that this treatment may lead to the pocketing of the peritoneum at the point of anchorage.

and invite recurrence. Passing the suture through and over the muscles may also interfere with the action of the muscles and weaken them by strangulation.

The complete removal of the hernial sac and closure of the internal abdominal ring are essential for a successful operation for oblique hernia. In the closure of the ring both arms and the angle of the ring should be identified. This can be done by elevating the spermatic cord and freeing adhesions beneath the cord by sponge dissection down to the angle of the ring. The angle of the ring will appear as dense fibers firmly adherent to the bed of the transversalis fascia. From this point each arm of the ring will be seen to run in line with its normal position. To facilitate the exposure of each arm, an Allis clamp may be placed on its fibers, and with elevation of the clamp the respective arms will come into view (Fig. 7). After such exposure the arms of the ring are approximated by two or three interrupted sutures above the cord. In placing the sutures one should avoid incorporating the spermatic cord tissues or closing the ring so tightly as to constrict the cord.

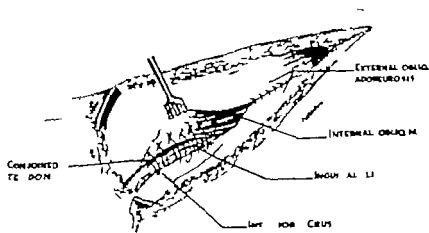
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For statistical purposes the size of the hernial defect may be obtained by a linear and transverse measurement of the defect using a graduated uterine probe.

Upon examination, the hernial defect may be found to be of such size that with retraction of the Hesselbach ligament and the aponeurosis of the transversus abdominis muscle approximating these structures to the superior tract and Cooper's ligament may lead to tension along the suture line. In such cases, Riethoff and others have suggested incising the rectus fascia at its pubic attachment, extending the incision in an upward manner for several centimeters (Fig. 7). This will provide relaxation of these structures for normal tissue closure. It has been found that such a procedure will not weaken the rectus muscle and the pyramidalis muscle support. However, in only one case in this series was a claying done on the rectus fascia found necessary, due to atrophy of Hesselbach ligament and the transversus abdominis aponeurosis following a previous operation for hernia.

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commencing the suture line over the pubic bone and passing the first suture through the lowermost portion of Hesselbach's ligament, Henle's ligament, and the iliopectineal tract, including Cooper's ligament and fibers of the lacunar (Gimbernat's) ligament (Fig. 7). It was found that this procedure accomplishes two things. First, the iliopectineal tract at its pubic insertion is often small and obscure lying beneath the inguinal ligament. The elevation of the iliopectineal tract by the suture will better identify the tract. Second, there is a better coaptation of the ligamentous structures. Occasionally the iliopectineal tract at its pubic insertion may be so obscure that it is difficult to recognize its fibers for placing the first suture. In such cases, before the suture line is commenced, the iliopectineal tract can be brought into clear view by passing the blunt end of the scalpel handle beneath the inguinal ligament opposite the pubic bone to separate the loose adhesions between the inguinal ligament and the iliopectineal tract. In this way the aponeurotic fibers of the iliopectineal tract will be clearly differentiated from the white fibers of the inguinal ligament. Utilizing the iliopectineal tract gives essential lateral support to the transversalis fascia.



— in its normal position, it represents the lower part of the external

muscle.

The suture, the femoral

the third

is approximately to the internal

The iliopectineal tract is continued in an upward manner to the abdominal ring (Fig. 7)

Totus and Jacob<sup>1</sup> in their anatomic description of the iliopectine tract and McVay and Anson,<sup>2</sup> discussing the clinical use of the iliopectine tract, have spoken of the diminution in the size of the tract as it crosses the femoral vessels (Fig. 7). It has been found, however, that the iliopectine tract is not altered at this point to such an extent as to interfere with approximation of the tract to Hesselbach's ligament and the transversus abdominis aponeurosis.

The operation is completed as follows. The spermatic cord and the ilio-inguinal nerve are replaced to the inguinal bed and permitted to rest on the utero line following the closure of the transversalis fascia (Fig. 8). The open or dead space above the pubic bone bounded laterally by the spermatic cord and the inguinal ligament, medially by the rectus fascia below and above and medially by the internal oblique and transversus abdominis muscles, is dealt with in the following manner. First if the case is one in which there is a congenital absence of the internal oblique and transversus abdominis muscles in the low inguinal space or atrophy of these muscles from disuse, nutritional deficiency or following necrosis secondary to previous surgery no attempt is made to close the space except loosely to approximate the muscle fibers of the internal oblique and transversus abdominis muscles to the inguinal ligament above the cord, opposite the internal abdominal ring. Second, if the internal oblique and transversus abdominis muscle fibers are healthy and well developed, they are loosely approximated to the inguinal ligament above the cord, opposite the internal abdominal ring as far downward as these muscle fibers extend. In closure of the fibers of the external oblique aponeurosis and the reconstruction of the subcutaneous ring care should be taken to avoid constriction of the spermatic cord or uterus (Fig. 8). Closure of Scarpa's fascia and the skin completes the operation.

#### SUMMARY

1 The recurrence following the standard (Bassini) operation for large oblique and direct hernia prompted the employment instead, of an operation utilizing the component part of the transversalis fascia and allied ligamentous structures in such cases. In 116 cases of large oblique recurrent and direct hernia in which this procedure was employed, questionnaires sent to the patient showed that there has not been a single recurrence of hernia in all questionnaires answered except three which were returned as unclaimed.

To further the knowledge of the deep supportive structures of the inguinal region an anatomic review has been made of these structures. This has consisted of a review of the literature in this field, cadaver research, autopsy, and clinical observation at operations.

2 The pathology of all inguinal hernia is not the same. To obtain the maximum result in the operation for inguinal hernia, it is necessary to consider the pathologic changes that accompany the different types of hernia in the inguinal support structures. Since the transversalis fascial support is not involved in the small oblique hernia usually seen in children, the treatment consists simply of the removal and closure of the patent processus vaginalis (see) down to the fold of the peritoneum and the closure of the internal abdominal ring as is employed in the Bassini operation.

4 The chief pathologic features in large oblique and direct hernias are the giving way of the transversalis fascial support and varying degrees of dilatation of the internal abdominal ring. Operations for these hernias should be directed toward restoring these structures to a normal state.

5 Special emphasis is placed on the importance of including the iliopectic tract in the suture line for closure of the transversalis fascia to maintain the lateral support of the fascia. In the oblique hernia, the dilated internal abdominal ring should be closed by identifying its arms and approximating them with interrupted sutures above the spermatic cord.

6 In the operative management, care should be taken to maintain hemostasis, thus preventing hematoma and serum accumulation which might invite infection and weaken the tissue support, and to avoid unnecessary trauma of the tissues, including the nerve supply which might result in weakened muscles. The operative field should be cleared of areolar and adipose tissues and struggling muscle fibers for good visualization and prevention of their incorporation in the suture line, which would weaken the ligamentous support.

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# A DEFINITIVE AMBULATORY TREATMENT FOR INFECTED PILONIDAL CYSTS

GEORGE CRILE, JR. M.D. CLEVELAND, OHIO

(From the Cleveland Clinic)

OPERATIONS for the cure of pilonidal cysts fall into two broad classifications (1) excision of the cyst with or without closure (2) marsupialization of the cyst with suture of the skin to the epithelium at the base of the cyst.

Excision of the cyst with primary closure is not applicable to acutely infected cysts because contamination and sacrifice of tissue result in a large infected dead space. Excision of the cyst and packing it open results in slow healing, and when the buttocks are fat it may be as long as a year before epithelization is complete. Moreover the ensuing scar is broad and is often painful and breaks down if traumatized. Marsupialization of the cyst with suture of the skin to the base sacrifices no tissue and results in faster healing. Even with this technique however the resultant wound takes weeks or even months to heal, requires many dressings, and causes prolonged disability.

The original epithelial rest is small and causes difficulty only because the denuded epithelium has no way of being discharged externally. To make an incision several inches long in order to marsupialize and provide drainage for a tiny epithelial rest seems unnecessarily radical. Before the cyst is listened by acute infection the epithelial rest is measurable in millimeters rather than in inches. If marsupialization could be effected by a conservative procedure and if following this the patient could be ambulatory and remain at work, a great economic saving would be effected.

The first patient that I treated by this method was W. on the U. S. N. Hospital Corps. He had had three operations for pilonidal cyst and developed severely infected recurrence. He did not wish to enter the hospital and could not consent further to treatment even if he did. I therefore drilled and irrigated the abscess. I left short sections of marshallows that he could use to maintain drainage.

The patient continued performing his duties on the ship and tolerated the marshallows rather about discomfort. Now the incision was large and the buttock was fat, I have had reason to be satisfied. After two weeks became apparent that epithelization was growing down the sides of the opening and in the end of three weeks his epithelization of the tract appeared to be complete. I the next day the cavity no larger than the marshallows of the catheter. There was no significant drainage. The catheter was removed and his skin is completely healed in and of below. Such a result that he only the rest is deep, complete epithelial discharge about 4 inches in diameter the base of which appeared to be the permanent of the scar. Follow up result on the patient for one year having been here no recurrence.

Since 1944 I have treated twelve patients with acutely infected pilonidal cyst by this technique with uniform success. There has been no recurrence and no complications. The retention catheter has caused no discomfort or disability. I have been tried to treat pilonidal abscess by this technique but with

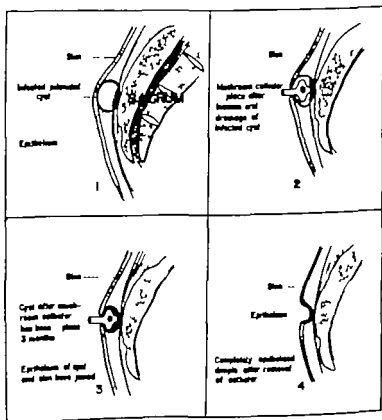


only indifferent results. It is difficult to get the tube in place and to maintain it in the proper position, and I doubt that the results will prove satisfactory. It is the acutely infected cyst that is ideally adapted to this technique.

### TECHNIQUE

The technique is illustrated in Figs. 1 to 4. The steps are as follows:

1. The skin is frozen with ethyl chloride.
2. An incision about  $1\frac{1}{2}$  cm. in length is made in the midline directly over what is estimated to be the exact center of the cyst.
3. The contents of the abscess are evacuated, and a mushroom catheter is inserted.
4. A safety pin is put through the catheter to prevent it from falling into the cavity and the tube is cut off distal to the pin.



→ make catheter at bottom of cyst  
 with mushroom catheter in place  
 in place three months wait epithelial-  
 ization of catheter

5. The patient is instructed to take sitz baths twice daily until the discharge diminishes.

6. At the end of one week the catheter is shortened and the safety pin is removed. The cavity by this time has diminished in size to such an extent that the catheter can be cut flush with the skin without danger of its falling back into the cavity.

7. The patient requires no further dressings or treatment for one month, at which time the catheter is again shortened by cutting it off flush with the skin.

8. At the end of three months the epithelium has grown down along the catheter and presumably has joined the epithelium growing in the bottom of the cyst thus marsupializing the cyst. The catheter is therefore removed.

9. Inspection at the end of one week shows nothing more than a deep dimple with its epithelized base resting on the periosteum of the sacrum. The patient is discharged.

From the economic standpoint this treatment has the following advantages: (1) no hospitalization, (2) no operation other than a simple office procedure, (3) only four postoperative office calls, (4) no dressings after the first week and (5) no loss of work after the first day.

From the standpoint of cure of the disease this treatment has the following advantages: (1) The epithelial rest apparently is completely and permanently marsupialized, (2) there are no painful dressings, (3) there is no deformity or scar other than a small dimple.

#### SUMMARY

A simple office procedure for the definitive treatment of acutely infected pilonidal cysts is described.

## ISCHIAL DECUBITUS ULCER

ERNEST BORG, M.D. AND A. ESTIN COMARR, M.D. VAN NUTE, CALIF.

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AMONG the recent references which deal with the management of decubitus ulcer<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11</sup> there are only four<sup>2, 3, 4, 12</sup> which mention the treatment of ischial bedsores. Since the incidence of ischial decubitus ulcers increases in proportion with the number of patients reaching the ambulatory stage it appeared worth while to report our experience in forty-one patients.

### INCIDENCE, DISTRIBUTION, SECONDARY BONE CHANGE, SIZE

Forty-seven ulcers were present in forty-one patients with spinal cord injuries. Among them there were only three cases not due to war wounds or war accidents. One cord injury developed after spinal anesthesia, another consequent to meningitis and epidural abscess, and a third was caused by a cord tumor.

Table I illustrates the level, date of injury, number of sores, types of intervention, and results in the respective cases.

The shortest interval before sores developed was three months and the longest was thirteen years. The duration of the sore prior to operation ranged from one month to three years.

There were two cervical, sixteen upper dorsal (first to sixth), seventeen lower dorsal (seventh to twelfth) and six lumbar lesions. No relationship could be established between the level of the lesion and the secondary bone changes. According to x-ray and biopsy findings bone involvement was present (Figs. 1 and 2) in thirty-five cases. The size of the ulcer varied from 2 by 4 cm. to 8 by 10 cm.

### ETIOLOGY

The etiology of decubitus ulcers has recently been discussed at length<sup>2, 3, 13</sup>. It has been pointed out that general factors such as hypoproteinemia<sup>2, 13, 14</sup>, exhaustion<sup>15</sup> and flare-up of infections<sup>16</sup> play a major role.<sup>14</sup>

response to histamine flare wheel and tach in the skin above and in cord lesion in all patients. T. B. Maxwell (personal communication of unpublished data) observed good circulation in granulations by the intravenous fluorescein method in six cases of cord injury with decubitus ulcers at DeWitt General Hospital, Auburn, Calif. in 1945. These findings are in contrast to the theory of locally disturbed sympathetic reflexes as an additional cause for the development of decubitus ulcer<sup>17</sup>. It is evident that the neurogenic factor plays an important role. It is responsible for loss of sensation, motor paralysis, and consequent drug trophic with decreased circulation of the subcutaneous

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structures. But the circulation of the skin itself does not seem to be impaired. Wherever continuous weight-bearing exerts pressure on a poorly padded skin area breakdown of the skin will ensue. This applies particularly to the ischial region. The majority of our patients displayed an atrophy of the buttocks. The precipitation of the sores was caused by prolonged sitting, by sitting in wet wrinkled clothes, or another local trauma. In contradistinction to the development of other ulcers after a sore-free interval, the ischial ulcer does not



FIG. 1.—B. H. \_\_\_\_\_, aged 4 years, level of the fourth dorsal vertebra, d. 14 of July April 1958. This is a large ischial decubitus ulcer with extensive involvement, calcification, and histologically proved bone metastases of bone on left prior to surgical repair.

reflect imbalance of the patient's health. Such ulcers develop by mere trauma in the absence of protein disturbances, anemia, or infection. It is furthermore obvious that ischial ulcers are preceded by a sore-free interval because there is no weight-bearing favoring their development.

#### ANATOMY PATHOLOGY HISTOLOGY GROSS APPEARANCE

The anatomy of the ischial region reveals the presence of bursae. Some authors describe the location of bursae as higher than the real point of

TABLE I

PRIMARY METHOD													STANDARD METHOD										
NAME	NUMBER OF FISSURES	INITIALS OF PATIENTS	AGE OF PATIENTS	DATE OF ENTRY	LEVEL OF ENTRY	QUALITY OF INC.	RIGHT OR LEFT	RESECTION OF CLAVICLE	HEALTH OF FISSURE	HEALING	TIME ELAPSED	HEALTHY TISSUE	NUMBER OF CLAVICLES	RESECTION	AT AGE	NUMBER OF FISSURES	LAST CLAVICLE	TIME ELAPSED	HEALTHY TISSUE	NUMBER OF CLAVICLES	RESECTION	AT AGE	NUMBER OF FISSURES
1	1	B B	24	1/45	D 15	Comp	Right	Yes	1	Exc	1	1 yr	Yes	1	Yes	Yes	1	Exc	6 mo.	N	1	1	1
2	2	L M	24	8/29/45	D 4	Comp	Right	Yes	1	Good	1	1 yr	Yes	1	Yes	Yes	1	Exc	6 mo.	N	2	2	2
3	3	P L	31	10/2/44	D 4	Comp.	Left	Yes	1	Exc	2 yr	2 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	3	3	3
4	4	B M	29	9/4/44	L-1	Inc	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	4	4	4
5	5	B M	29	9/4/44	L-1	Inc	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	5	5	5
6	6	B M	29	9/4/44	L-1	Inc	Left	Yes	1	Poor	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	6	6	6
7	7	P M	28	10/6/44	D 4	Comp.	Right	Yes	2	Poor	1 yr	1 yr	N	2	Yes	Yes	1	Exc	6 mo.	N	7	7	7
8	8	J P	29	5/—/45	L 8	Comp	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	8	8	8
9	9	H M	29	4/1/45	D 6	Inc	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	9	9	9
10	10	D D	28	3/2/46	L 2	Inc	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	10	10	10
11	11	M K	42	6/7/31	D 11	Comp.	Left	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	11	11	11
12	12	E K	29	2/4	D 4	Comp.	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	12	12	12
13	13	D L	29	4/2/45	L-1	Inc	Left	N	2	Poor	1 yr	1 yr	N	2	Yes	Yes	1	Exc	6 mo.	N	13	13	13
14	14	C V	29	9/11/44	L 9	Comp.	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	14	14	14
15	15	M T	29	6/1/44	D 11	Comp.	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	15	15	15
16	16	G L	49	7/26/44	D 15	Comp.	Right	N	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	16	16	16
17	17	M D	32	6/4/45	D 4	Comp.	Left	N	2	Exc	1 yr	1 yr	N	2	Yes	Yes	1	Exc	6 mo.	N	17	17	17
18	18	O H	28	11/11/43	D 11	Inc	Left	Yes	2	Exc	1 yr	1 yr	N	2	Yes	Yes	1	Exc	6 mo.	N	18	18	18
19	19	D R	24	4/2/45	D 4	Comp	Right	Yes	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	19	19	19
20	20	D R	24	4/2/45	D 4	Comp	Right	Yes	1	Exc	1 yr	1 yr	N	1	Yes	Yes	1	Exc	6 mo.	N	20	20	20

No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
1	2	3	4</																											

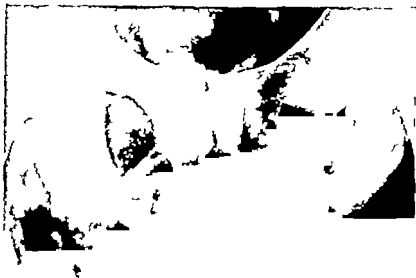


Fig. 2.—Same case as Fig. 1 four weeks after operative repair on the left. Some microblasts remain between the muscle planes but labial contour is smooth. Right side is unchanged.



Fig. 3.—H. M. aged 28 years, level of the earth dorsal vertebra, date of injury Oct. 6, 1944. Right labial decubitus ulcer with slight periosteal proliferation and bone exposure. Contact of labial tuberosity causing ulceration.

contact on sitting. Whereas the *bursa musculi glutaei maximi* lies between the muscle and the tuber ossis ischium the *bursa musculi bicipitis superior* separates the long head of this muscle from the ischial tuberosity. At times only subcutaneous tissue separates the skin from the periosteum. Trauma with initial ischemia is quickly followed by necrosis and infection. This may spread into preformed bursae and may even travel along muscle planes to adjacent structures, especially to the ischio-rectal fossa.

The poor vascularization of this region with its predominance of fatty tissue accounts for the low degree of resistance. Infection of the periosteum is followed by periostitis and osteitis in the spongy bone structure of the tuberosity (Fig. 3). The proximity of the anus favors continuation of infection. The bacterial flora encountered in this group of cases consisted of *Pseudomonas aeruginosa* hemolytic, *Staphylococcus aureus*, beta streptococcus, *Corynebacterium*, *Escherichia coli*, *Bacillus proteus* and *Campylobacter*. This corresponds with the findings of other authors. The microscopic findings revealed chronic inflammatory non-specific granulation tissue with hyaline coagulation necrosis and infiltration with round cells with occasional eosinophiles. The picture was essentially dense fibrous tissue and capillary proliferation. Frequently calcific deposits were found which had undergone metaplastic ossification and cartilage formation (Fig. 4 A and B).

The gross appearance varies. There are ulcers of long standing which reveal only a small ulcer opening leading into the bursal sac (Fig. 5) while there are others which show a large area with undermined edges and exposed deep structures (Fig. 6). The various stages from the early superficial bruise to the final fully developed ulcer are like those generally observed in sores in any other location. The enumerated anatomic facts and the additional impairment of blood supply by dense atrophy explain the lack of an efficient defense barrier. They also explain why conservative treatment with penicillin jelly, Furin, granulated sugar or cod liver compound is ineffective while it yields good results in bone lesions or other decubitus ulcers.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup>

#### PREOPERATIVE TREATMENT

The preoperative treatment is essentially the same as in ulcers of other locations.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> It is directed toward improvement of the general and local condition. Anemia must be corrected first especially in the presence of hypoproteinemia because protein administered is less well utilized for restitution of hemoglobin.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> The protein loss from sores has been found to be as high as 50 mg.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> A reversed albumin to bulbo ratio suggests a depletion in proteins.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> The importance of a positive protein balance has been stressed.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> Therefore amino acid should be administered by mouth and vein in cases of deficiency.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> But even in the presence of a positive protein balance and a normal blood count regular blood transfusions before and after one to two times per week starting two weeks prior to intervention and continued for two weeks after operation, have proved very satisfactory. In addition, avitaminosis must be corrected.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100</sup> Insulin was recom-



A



Fig. 1.—1. R. H. Sand 2. A. level of the fourth dorsal vertebra, date of injury April 2. 3. Left lateral thoracic nerve. (paraffin, tol. stain, X10 showing calcium deposits with metaplastic bone formation. 4. Hematoxylin and eosin, X 60 showing neurotrophic spread of skeletal muscle fibers with increase of cytoplasmic staining.

PL 8



mended in the presence of anorrhexia. Systemic penicillin and sulfadiazine (where tolerated) are started twenty-four to forty-eight hours prior to surgery. <sup>23, 24, 25</sup>

The local treatment consists of repeated debridement followed by Dakin irrigation through tubes with protective zinc oxide ointment for the skin. Other authors recommend hypertonic saline solution and aluminum acetate, tyrothricin gauze-mesh, or specific local therapy with antiseptics. In the absence of enough good granulations are maintained by wet dressings of Domeboro's solution. No attempt was made to sterilize the ulcers in concurrence with some<sup>2, 4, 5, 12</sup> and in contrast to other authors<sup>6</sup> who defer operations in presence of certain microorganisms. When no necrosis is present the granulation tissue appears strong and healthy with marginal epithelialization there is a positive nitrogen balance and a gain of weight, the patient is ready for surgery. <sup>13</sup>

The general postoperative management is continuation of the preoperative regime. Penicillin and sulfa therapy are carried out for ten to fourteen days. Blood transfusions are administered once or twice a week. The drains are loosened after three to four days and removed around the fifth day. The sutures are removed after ten to twelve days except the retention sutures which are left in place as long as necessary—open up to fourteen days.<sup>2, 26</sup> During the entire postoperative period no weight bearing is permitted for at least six weeks. Frequent change of position is carried out but no plaster immobilization is used.

#### SURGICAL TECHNIQUE

The lesion is excised en bloc from a transversal approach, parallel to the crease. If the bone is not involved, only the bursa is excised and the gluteus maximus muscle pulled over the tuberosity by interrupted chromic 0 sutures. In cases of bone involvement (primary method) again an attempt is made of removal en bloc but this includes the periosteum and bone (Figs 7 and 8). Free use is made of chisel and rongeur. The bone should be smoothed after its healthy parts have been reached. It is covered by muscle in two different ways. Where there is a well-mobilized gluteus it can be approximated by an inverting suture of 01% stainless steel wires on buttons (Fig 9A primary method). Where muscle is not redundant when there is a recurrence of the ulcer a small pedicled flap of half the thickness of the gluteus maximus is formed and there is rotated into place to cover the bone and is attached to the surrounding structures by chromic catgut sutures (Fig 9B secondary method). Both methods aim at adequate muscle padding of the residual bonyity.

Hemostasis is achieved by electrofulguration, hot saline pads, and plain 00 catgut for major vessel. Preferably one or two drains are used. Retention sutures on buttons are used where indicated. Stainless steel 002 and 003 are used for the skin. A fluffy gauze compression dressing is applied with elasticoplast reinforced by an elastic ACE pipe bandage.

<sup>23</sup>The Domeboro solution consists of 10 g of zinc oxide, 10 g of aluminum acetate, and aluminum sulfate. One tablet dissolved in 1 liter of water. Solution of aluminum acetate 1/100 which is free from lead. One-half of the normal strength as used in the reported cases.

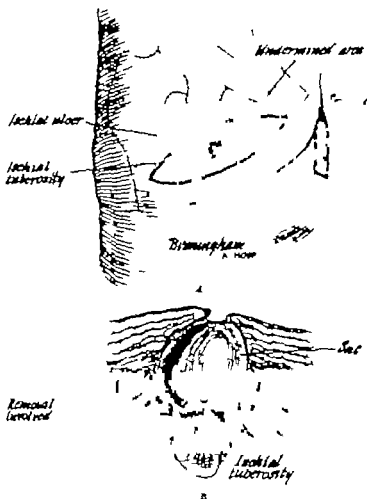


Fig. 1.—Outline of elliptical skin excision in order to reach the ulcer zone to the bone. A. Frontal. B. Transverse. (Line of removal of bone is function of ischial sac.)

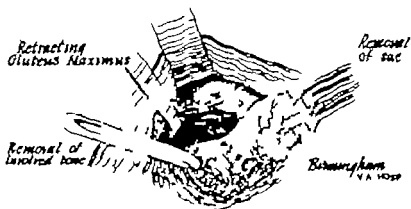


Fig. 2.—Removal of entire sac with adherent bone.

## RESULTS

The results are evident from Table II. The total cures with all methods were 85.1 per cent, the total of failures was 13 per cent. 66 per cent responded with healing to one operation and 19 per cent closed after repeated operations. The breakdown of cures with the simple primary method as compared with the pedicle muscle flap reveals 62.5 per cent against 79.4 per cent, and is in favor of the pedicle muscle flap. If one compares the recurrence rate based upon the

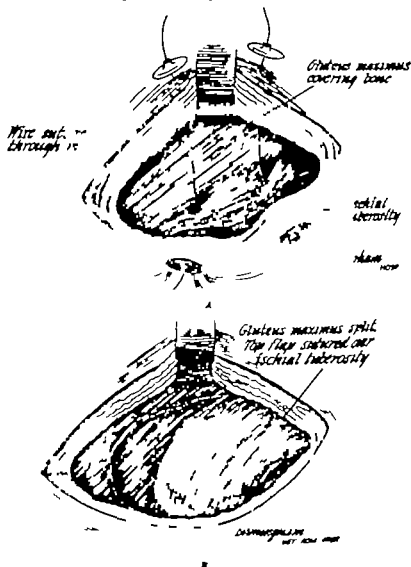


Fig. 1—A. Primary Method. B. Secondary Method. Both show stainless steel wire in cut the pedicle flap and loop B in place in order to cut the ischial tuberosity. B. Secondary Method. Muscle flap with medial pedicle half thickness of gluteus muscle rotated in place to cover ischial tuberosity.

number of patients rather than number of ulcers one finds an even more favorable figure of failure in only 1.3 per cent with the pedicle procedure as against 28.6 per cent with the primary method.

The seven failures comprise those ulcers which up to date did not heal. One case was due to faulty interpretation of the x rays (Fig. 3). The bone changes remained unrecognized and untreated. The second case ended in failure of both methods due to many incisions. The patient fell out of bed another time became too painful and was not immobilized enough and finally a technical error prevented the desired result. Although the sore closed by granulation and buried epidermis graft the case was considered a failure. Prolonged sitting and a periprostitis produced two recurrences in the third patient whose ulcer stayed closed for periods of three months. Two patients were uncooperative and sat for periods of more than eight hours driving their cars. The pedicle flap withstood this trauma but the skin broke down. A sixth case failed due to a postoperative hematoma despite drainage and the seventh patient had to go on an empysemic leave before a stable scar developed.

TABLE II

	NUMBER OF CASES	PER CENT
Set (cases) the II method	26	91.1
Total cases the same operation	28	96.9
Total cases floor operation	3	19.6
Total failures	7	25.0
Total	28	100.0

TABLE III: BY METHOD (1 CASES, 4 ULTERS)

	NUMBER OF CASES	PER CENT
Excellent (about recurrence)	13	65.0
Primary (without the II method)	4	10.0
Good (about recurrence)	1	4.0
Good (b. m. m. m.)	1	4.0
Poor	3	12.5
Total	22	100.0

TABLE IV: BY METHOD (1 CASES, 22 ULTERS) OVERLAPPING OF BOTH METHODS

	NUMBER OF CASES	PER CENT
Excellent (no recurrence)	1	4.5
Excellent (b. m. m. m.)	1	4.5
Good (no recurrence)	2	9.1
Good (b. m. m. m.)	1	4.5
Poor	18	81.5
Total	22	100.0

No relationship between the duration of an ulcer and the outcome of treatment could be established.

The result was called excellent in the presence of primary union, good when a small separation of the suture line occurred (1 to 2 cm.) which closed by delayed healing and poor where a frank nonunion persisted.

TABLE IV

Freeman mentioned in cases with breakdown after skin flap procedures but did not give the total number of rectal ulcers. White and Hamm<sup>12</sup> re-

ported one case, Croce and Beaker<sup>17</sup> nine cases, four of the patients operated upon with two cures and two failures, and Conway and co-workers<sup>2</sup> 30 cases, fifteen of the patients operated on. Conway and co-workers stated that they had seven cures and eight failures. Our figures therefore compare favorably with those of other authors.

The incidence of ischial ulcers based upon the total number of sores was given as 10 per cent by Conway and co-authors. Our observations concur with their findings. However if based upon the number of patients our figure would be about .3 per cent. It is to be expected that this ulcer as a late sore will occur even in well balanced patients at any time. It may recur even after a sore-free interval of one year or longer. The patients must abide by their instruction for preventive measures. It also will be difficult to analyze what ought to be called a recurrence due either to inadequate operative procedure or to negligence on the part of the patient.

Skin flap methods have been advocated generally in the literature<sup>4, 11, 12</sup> against linear incisions in the treatment of bedsores. However it has been stated that a flap can break down<sup>13</sup> and we confirm this experience. We feel that the muscular padding of ischial ulcers establishes a workable compromise between an internal flap and an external linear incision. Osteotomy is essential in the management of ischial ulcers, and where possible this should be done en bloc with the bursa. Conway and co-authors have recently recommended osteotomy in ulcers of different localization.

Different kinds of suture material have been used by various authors. Cotton,<sup>14, 15, 16</sup> tantalum, and stainless steel for tension sutures<sup>10</sup> and ligatures<sup>17</sup> represent the nonabsorbable material. Plain gut and chromic catgut<sup>4, 11, 12</sup> were used as absorbable material. Silk,<sup>4, 11</sup> horsehair<sup>11</sup> and waxed silk<sup>14</sup> have been used for the skin. From the results reported it appears that it is not essential what material is used. Waxed silk or stainless steel<sup>12, 16</sup> with its resistance against body fluids and absence of capillary action. We prefer electrocautery for hemostasis in concurrence with Gibbon and Freeman<sup>18</sup> even though it has recently been rejected. We also agree with the experience<sup>13</sup> that the bacteriologic flora does not play a decisive role. Proper postoperative position and immobilization are important. We have not yet adopted the plaster of Paris spica<sup>19</sup>. Weight-bearing prior to six weeks postoperatively jeopardizes the result.

In order to prevent the development of ischial sores rather than to derive better means of therapy it is necessary to teach the patients how to achieve this goal. Medical instruction to the individual patient and to the paraplegic patients as a group has been attempted. This is the more important because of the psychology of the paraplegic patient which follows its own pattern.<sup>20</sup> The prevention consists of taking off the weight at regular intervals while sitting and the early use of braces.

When an ulcer has developed its treatment will be indicated along the following lines: a simple ulcer with bursa formation could be treated by excision; a primary ulcer with bone involvement and ample redundant gluteal musculature

lature is approached by the primary method. All other conditions, especially recurrences, should be treated by the radical secondary method with a pedicled muscle flap.

#### SUMMARY

1. Forty-seven ischial ulcers are presented in forty-one patients.

2. The sore-free interval from the time of injury to the onset of the ulcer ranged from three months to thirteen years.

3. There were two cervical, sixteen upper dorsal, seventeen lower dorsal, and six lumbar lesions. Secondary bone changes were present in thirty-five cases but no relationship between level of injury and secondary bone changes could be established.

4. Local trauma plays the major role in the etiology of the ischial ulcer. It is believed that the skin circulation is unimpaired but that the neurogenic disuse atrophy of the underlying structures is a contributory factor. This late ulcer might develop in the absence of protein disturbances, anemia, or infection.

5. The tendency of the infection to spread to deeper tissues is favored by the presence of poorly vascularized bursa and the proximity of the anus. True metaplastic ossification and cartilage formation is found on histologic examination. The bacterial flora is similar to that encountered in the concurrent urinary infection. Conservative treatment of a fully developed ulcer is unsuccessful.

6. The local preoperative treatment consists in debridement. The general preoperative treatment should correct hypoproteinemia, avitaminosis, and anemia. Multiple blood transfusions are beneficial even in the absence of hypoproteinemia or anemia. Sulfonamides and penicillin are used systemically. Postoperatively a similar regime is carried out as preoperatively. Sutures are removed at a late date.

7. Two methods of surgical treatment are presented. Both remove the ulcer en bloc including the bone. The primary method uses the redundant gluteal musculature for the covering of the bone defect by an inverting stitch of stainless steel wire. The secondary method uses a pedicled gluteal flap for the padding of the bone. Stainless steel is used for skin closure. Drainage is important.

8. The total number of cures was 85.1 per cent, the total number of failures, 15 per cent. 66 per cent healed after one intervention, 19 per cent needed more than one operation. The number of cures with one intervention and the number of recurrences is in favor of the secondary method. The causes of failure were faulty interpretation of x-rays, technical errors, lack of immobilization, and lack of cooperation of the patient.

9. The results presented and the technique are discussed in the light of the recent literature.

10. Early use of braces and medical instruction of the patients are recommended for the prevention of ulcers.

11. A simple ulcer with bursa formation is excised. A primary ulcer with redundant muscle and bone involvement is treated by the primary method and all other conditions by the secondary method.



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When an ulcer has developed, its treatment will be indicated along the following lines: a simple ulcer with bursa formation could be treated by excision; a primary ulcer with bone involvement and ample redundant gluteal musculature

## ON THE HISTOLOGY OF SURGICALLY REMOVED SYMPATHETIC GANGLIA

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SINCE the etiology and underlying pathology of disorders such as essential hypertension and peripheral vascular disease are but poorly understood, it is not surprising that specimens removed by sympathectomy have been examined with a great deal of curiosity. Even before sympathectomy became a well-established procedure, pathologists were attracted by the increasing evidence of the important role the autonomic nerves play in health and disease and histopathologic studies of sympathetic ganglia gained at autopsies were carried out. The interest was limited between the neuronal structures and the interstitial and vascular tissues of the ganglia. Many investigators have shown that ganglia are prone to exhibit a variety of histopathologic findings. They list in one form or another the disorder and coexistent changes with or without advancing hypotheses.<sup>1-15</sup> Even authors who lean toward the post hoc propter hoc view and consider the underlying pathology of a case responsible for the histologic changes in the ganglia are constrained to qualify their conclusions.

The main difficulty in judging changes in sympathetic ganglia lies in setting down standards of normalcy by procuring suitable controls. Perfectly healthy persons remain in possession of the sympathetic ganglia, while autopsy material stems from patients with some fatal disease or from victims of accidents, where an exact history, data on blood pressure, etc., is rarely available and is often improperly fixed for careful histologic purposes.

Another pitfall in evaluating the histology of human sympathetic ganglia is the mistaking of changes due to age for pathologic alterations. Age changes simulate or may be identical with pathologic lesions and in many instances it remains a matter of speculation or definition how to classify a certain abnormal picture. It has been established by many investigators

who studied from various angles the changes in the human nervous system, that conspicuous changes begin to appear after the second decade of life and progress into old age.

Critical evaluation of the literature leads to the sobering conclusion that almost every finding in ganglia from patients suffering from a certain disorder can be observed in ganglia of persons not afflicted with the disease in question.

The present studies were not aimed at a statistical analysis of the material at hand. The purpose was to examine carefully the histology of a limited number of operative specimens, that is, ganglia removed to alleviate hypertension.

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gress strictly with age: no adult ganglion shows the delicate net of vessels found in children. Ganglia from senile persons tend to exhibit a scanty vascular bed.

Within the ganglia one sees many vascular lumina encased in a thick hyaline wall (Figs 5, 7, and 8). They were found in the majority of patients who had suffered from essential hypertension or peripheral vascular disease. They were absent in all children and young persons, including two patients, 21 and 33 years of age, on whom a lumbar sympathectomy had been performed for peripheral vascular disease. The vessels thus affected do not show an internal elastic membrane; rather their media consist of a hyaline mass, exceedingly

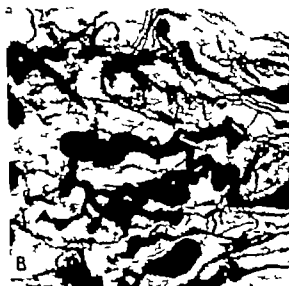
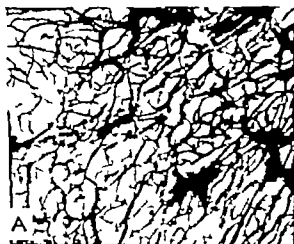


Fig. 1.—Vessel in sympathetic ganglion of 18-month-old male infant (swainson-stained paraffin). (Hemalum stain,  $\times 100$ ). B: Vessel in sympathetic ganglion of 33-year-old male with rheumatic heart disease. (Eosin-stained paraffin). (Hemalum stain,  $\times 100$ ).

or peripheral vascular disease. The pictures obtained with a variety of histologic stains were then compared with control material, as set forth in the following two paragraphs. A thorough analysis of a larger number of cases and a more detailed correlation with data in the literature are being planned.

#### MATERIAL AND METHODS

The specimens gained by twenty-four sympathectomies consisted of sympathetic ganglia, chain, and splanchnic nerves where a thoracolumbar sympathectomy was employed (fourteen cases). Lumbar chain and ganglia removed in ten instances for treatment of peripheral vascular disease form the other part of the material. The age of the patients ranged from 21 to 67 years. Several specimens from hypertensive patients were used. The material was fixed directly after removal, most in 10 per cent formalin, some in acid alcohol, and embedded in paraffin. Bodian's activated protargol, Mallory's aniline blue Verhoeff's elastic tissue stain, cresylviolet and hematoxylin-eosin were used routinely. Separate blocks of chain and splanchnic nerves were stained with osmic acid. Parts of ganglia were used for frozen sections, 300 to 400 micra thick, to visualize the vascular pattern by means of the benzidine technique of Doherty, Suh, and Alexander.

Material from forty-one autopsies of patients ranging from newborn to 83 years of age tabulated in Fig. 1 and consisting of celiac and sympathetic chain ganglia had been collected some years before in the Boston City Hospital for their investigations. This control material was prepared with similar techniques and it proved to be valuable for comparison, since it contained many specimens from patients who had not suffered from peripheral vascular or hypertensive disease.

#### OBSERVATIONS

**The Vascular Bed.**—Thick frozen sections stained with benzidine reveal the vascular pattern characteristic for ganglia. A dense regular network appears in children, Fig. 1, A, tortuous channels of varying diameters are found in young individuals, while around the twentieth year the irregularities in diameter assume the shape of spindles, ampullae and spherical dilatations which become well marked in adult and aging persons (Figs. 1, B and 2). In hematoxylin-

layer surrounded the intimal lining. They occur only within the ganglia and are probably responsible for the statement of pathologists who describe congested vessels, hyperemia, and increased capillary bed,<sup>4</sup> an impression based on examining only stained thin sections. The 300 to 400 micra thick slides of tissue here presented disclose the vascular tree in three dimensions. The vascular pattern appears to be independent of the underlying pathology and more nearly related to age. Although the size and number of the vascular dilatations do not pro-

\*Generous contribution by Dr. R. H. Smith, M.D., Boston.

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gress strictly with age; no adult ganglion shows the delicate net of vessels found in children. Ganglia from senile persons tend to exhibit a scanty vascular bed.

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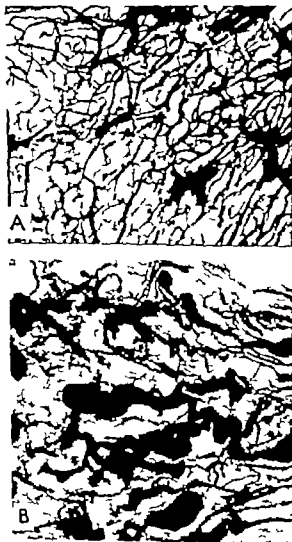


Fig. —4. Vessels in sympathetic ganglion of 16-month-old male infant (meningo-  
carcinal process). (Paraffin section,  $\times 7$ ). B. vessel in sympathetic ganglion of 1-year-old  
male with rheumatic heart disease. (Thionin stain,  $\times 60$ ).

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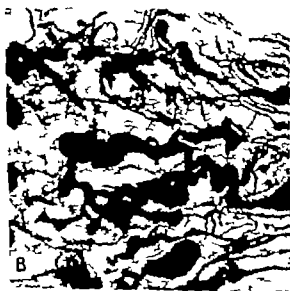


Fig. 1—4. Vessels in sympathetic ganglion of 15-month-old male infant (Hematoxylin-  
eosin stain). Fig. 5—7. Vessels in sympathetic ganglion of a 41-year-old male with rheumatic heart disease (Hematoxylin stain,  $\times 200$ ).



poor in, or entirely devoid of, nuclei. Aniline blue preparations show that these hyaline areas contain loose smokelike strands of reticular fibers (Fig. 6). Transitions from normal capillary or venous walls to fibrous thickenings up to the described hyaline halos do exist. It is of interest that sometimes hyalinization apparently encroaches on the environment of the vessels so that a vessel may appear to lie within an irregularly shaped halo of an almost structureless mass. A portion of the circumference of the vascular wall may remain normal while the remainder exhibits hyaline projections. It is possible to trace some of these vessels into extrinsic veins. The hyalinized tissue then blends with the fibrous capsule of the ganglion. Outside the ganglion the vein retains its normal delicate wall.

Although the arterioles within the ganglia removed at operation may show hyaline walls and/or intimal thickenings, some severe cases of essential hypertension revealed only normal arterioles in the ganglia. In general, arteriolar changes were much less frequent than hyaline halos observed about the capillary or venous channels.

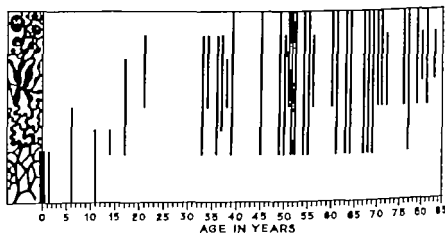


Fig. 2—Graph showing types of anatomic patterns in sympathetic ganglia of forty-one autopsy cases. The thick line at age 0 indicates four newborn infants.

**Infiltrating Processes.**—Unremitting loci of cellular infiltrations are common findings in the ganglia described in the literature as well as in the material at hand. Round cells or polymorphonuclear leucocytes, or both are found to form dense perivascular cuffs, larger areas of infiltration covering nerve cells, fibers, and vessels. They sometimes lie within the wall of a vessel and can be continuous with intra- or extravascular infiltrations. Control ganglia of children and young persons did not show cellular aggregates, but they were lacking as well in some old individuals, including hypertensives and patients with peripheral vascular disease. In Staemmler's long list the incidence of inflammatory infiltrations increases with age. In our material no connection between sympathetic ganglionitis and clinical diagnosis of the individual case could not be established.



FIG 3.—Low magnification view of thin section from lumbar sympathetic ganglion of 22-year-old man with lumbar sympathectomy and peripheral vascular disease (H&E stain, X 74).

Fig. 3.—Low magnification view of thin section from lumbar sympathetic ganglion of 22-year-old man with lumbar sympathectomy and peripheral vascular disease. A. acinar and nerve cell is seen. (H&E stain, X 74).

Fig. 4.—Thick and all of intravascular space in lumbar sympathetic ganglion of 22-year-old man with lumbar sympathectomy and peripheral vascular disease. H&E stain (H&E stain, X 74).

Fig. 5.—Thick and all of intravascular space in lumbar sympathetic ganglion of 66-year-old man with lumbar sympathectomy and peripheral vascular disease (Bodian silver method, counterstained with fast green).

**The Intercellular.**—The connective tissue of ganglia consists mainly of its outer collagenous and elastic capsular septa and perivascular sheaths. The reticulum and other framework tissue increases in coarseness and density with age. In extreme cases one can observe veritable fibrosis of a ganglion at the expense of neuronal elements. Whether or not this situation is due to inflammatory processes, as claimed by Staemmler, requires verification. Children's ganglia excel in delicacy and sparsity of framework tissue. The sheaths of key Retzius and the reticulum around the capillaries are loosely woven, while in adults the framework is denser, coarser and more extensive. The degree of fibrosis in older persons, however, did not correspond exactly with the severity of vascular alterations or the incidence of infiltrating processes.



FIG. 7

FIG. 8

FIG. 7.—Irradiated pigmented ganglion cell and hyaline capsule from superior bulbous portion of 7-year-old son of the author, sympathetic and peripheral (Hodgson's method counterstained with fast green) (X325).  
 FIG. 8.—(Greatly thickened) irregularly shaped cell from same portion of same bulbous portion of 17-year-old son of the author (Hodgson's method counterstained with fast green) (X325).

**The Neurons.**—Cresyl violet stained sections of sympathetic ganglia reveal a great variety of normal cells, interspersed among a majority of normal elements. Paucity of Nissl substance, accumulation of H. bodies, chromatolysis, swollen pale cells and posterior cell capsules containing foam detritus, pyknosis or absence of nuclei, ghostlike cell shadows, and decrease in the number or density of satellite cells are the most common findings. We did not feel justified in following Laignel-Lavastine<sup>14</sup> who considered marginal position of the nucleus and even eccentric position of the nucleolus as abnormal. The incidence of cellular changes is exceedingly low in the child. In autopsy and peritaph material gained from adults, the correlation with age and diagnosis accorded to Hunt<sup>15</sup> and Kuntz and Sulzberg<sup>16</sup> the appearance of the Nissl substance and of the satellite cell changes with the functional state of the cell. It was possible to see in our series alterations they described, but since normal elements

could always be found in the same ganglia and since presumably normal individuals also showed similar pictures, we were reluctant to draw any conclusions. Bodian's silver stain applied to ganglia gives a similar variety of abnormal findings. Heavy load of argyrophil pigment in neurones of adults, haphazard or absence of neurofibrillar structure, thickening of dendrites, and focacitation of nerve cells can be seen. Knotted and beaded axones, indicating degeneration, were observed singly or in strands. The pictures seen correspond to the forms described by De Castro in his account of normal and pathologic sympathetic neurones. Bimucleated nerve cells can be found in all age groups (Fig 7). Their significance is discussed by Beaton, Holmes, and Windle. There is no evidence that they represent pathologic forms. A somewhat aberrant type of cell was met in most of the silver preparation. They were smaller than the average nerve cell, round or polygonal with blunted corners, apparently without processes. The nucleus was denser than that of ordinary neurones, the cytoplasm homogeneous without fibrils, but occasionally laden with argyrophil granules, finer than the pigment in typical nerve cells (Fig 8).

#### COMMENTS

The results indicate that the histology of sympathetic ganglia does not give us information about the severity of vascular disease. Although the hyalinized vessels in our series were best developed in some cases with Buerger's disease differentiation of essential hypertension from peripheral vascular disease is not possible since hyalinization is a common finding in either one of the two groups of patient. The severity of the disease as judged by duration, blood pressure, and clinical course is not proportionate to the degree and extent of morphologic alterations. It appears rather that the ganglia are not a sensitive gauge for recording the diseases in question since they suffer to a varying degree under pathologic and aging processes of the entire organism. More light could be shed on the histopathology of sympathetic ganglia by accumulating more control material from aging persons not afflicted with vascular disorders. A critical evaluation of the literature together with our findings lead to the conclusion that there is no specific histologic picture of hypertension or peripheral vascular disease in sympathetic ganglia. This harmonizes with the view that sympathectomy, although a valuable aid in denervating the vascular bed or interrupting harmful visceral reflexes, probably does not constitute an attack against the source of vascular disease.

#### SUMMARY

1. Ganglia removed by sympathectomy and stained by a variety of techniques have been compared to routine autopsy material of known age and diagnosis.

Abnormal findings in sympathetic ganglia of adults are exceedingly common and include degenerating neurones, inflammatory infiltrations, in reaction to

cells of intrinsic veins

little connective tissue delicate



## INTERNAL FIXATION OF HIP FRACTURES WITH A NEW LAG SCREW

JOHN S. LUNDHOLM, M.D. ROCKFORD, ILL.

**FRACTURE** of the neck of the femur is the most common accident occurring in later life and is one of the most serious injuries that befall the elderly. Until as late as 1875 when Smith Petersen presented the three flanged nail and thus gave impetus to the real development of modern fixation methods, the great majority of these fractures terminated finally in death. The truth of this statement is attested by the fact that in most countries in this country a death occurring within one year following hip fracture must be reported to the coroner of the county in which the death occurred.

The history of treatment of fractures of the hip comprises a voluminous literature and through it all the method of internal fixation has become an approved and accepted treatment with a large percentage of excellent results and a gratifying drop in mortality rates. Particularly in intracapsular types of fracture internal fixation proved its value and prevented distressing non-union.

The lag screw has long been used by mechanics to approximate surfaces when it is impossible or inadvisable to use a bolt. The application of the principle of the wide flanged thread of the lag screw to bone surgery is particularly logical in that it serves to hold the fractured ends more firmly together than any other fixation medium. This was recognized many years ago by Johansson when he brought forth his bone screw and later by many other surgeons. I have used the lag screw herein described for more than six years and have not found a single instance in which the screw has slipped, or rotation has occurred. On the contrary, when reduction of the fracture is accurate the two fragments are held in such firm apposition that rotation is not possible. In several cases where bone resorption and absorption occurred I found the lag screw still held the fragment in exact position eventually resulting in good union in good position. No force is required in the insertion of the lag screw, therefore no impaction occurs and there is no danger of splitting the shaft when going through the hard cortical bone of elderly patients.

The lag screw herein presented fulfill the criteria of rigid fixation as laid down by Watson Jones a number of years ago, namely:

1. Rotation of fragments should be prevented
- Length of joint should be sufficient to prevent angulatory movement
2. There should be a minimum of bone displacement
3. There should be a maximum of bone surface contact

The lag screw is constructed of non electrolytic nonmagnetic molybdenum stainless steel in varying lengths to meet the variation in size of femurs. The

principle of drawing the two fragments together requires that all of the threaded portion of the screw should be in the proximal fragment. After careful study and measurement of a large number of hip fractures I found that the proximal fragment was invariably a minimum of one inch in length. Because of this constant finding the threaded portion of the screw is less than one inch in length, which suffices for all hip fractures regardless of where the line of fracture runs. The head of the screw is beveled at 130 degrees, which is the average approximate angle of the femoral neck to the shaft. This permits the under surface of the screw head to lie flat against the shaft instead of digging sharply into the bone. Instead of the conventional slot for the insertion of a screw driver a hexagonal shaft is countersunk in the head into which the hexagonal bar of a special screw driver is illustrated, that of an ordinary Allen screw fits securely. This gives complete control of direction and lever arm without danger of slipping or sliding of the screw driver.

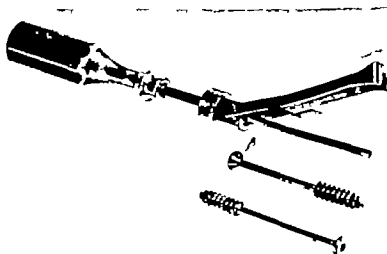


Fig. 1.—Illustration of hip screw herein described. This type of screw driver used. This hip screw is made of nonferrous stainless steel which is nonmagnetic and non-electrolytic.

The time to operate is always a question of clinical judgment depending entirely upon the condition of the patient, the type of fracture and the presence or absence of complication. There is usually no need of haste. I have found it most satisfactory to operate within the first twenty-four hours of collision when it is possible. In the presence of shock, internal injury, or complications, it is sometimes advisable to delay fixation for a few weeks. During this interim the patient should be kept comfortable as possible with bandages or their equivalent holding the injured leg or in some cases light traction. Anesthesia is purely a matter of choice although spinal or caudal procaine or intravenous Pentothal sodium is advisable if the operation is to be performed on the x-ray table.

## TECHNIQUE

The patient is brought to the operating room following the usual preoperative medication and is placed on an ordinary operating table. A cassette holder replaces a part of the mattress pad to facilitate the taking of films during the progress of the operation but no other special equipment is needed.

The patient is then anesthetized and reduction of the fracture accomplished by the Leadbetter method or any other successful maneuver. I have personally used the Leadbetter method and have had no difficulty in reducing all fractures. The thigh is flexed to 90 degrees with the knee also flexed to 90 degrees. A folded towel is passed around the upper thigh and traction is applied by an



Fig. 2—A, Intertrochanteric fracture of right femur. B, fracture reduced and fixation with lag screw accomplished.

assistant holding this towel while manual traction is also applied in the axis of the flexed thigh. With traction being applied in these two directions the thigh is internally rotated and the leg is slowly circumducted into abduction and brought out the internal rotation being maintained. As the leg is brought down to table level the foot is just over the lateral edge of the table and the heel palm test is applied to confirm reduction. A nurse or orderly then holds the leg in this position throughout the operation and x-ray views are taken in



both anteroposterior and lateral planes to ascertain that the fracture has been reduced.

The technique of taking satisfactory roentgenograms in both planes is relatively simple. The cassette holder on the operating table is adjusted to hold a cassette under the pelvis and a loaded cassette is inserted. For the anteroposterior view the tube is centered over the neck of the femur using the following landmarks. In draping the patient a towel clip is clipped through the sheets and into the skin at a point midway between the symphysis pubis and the anterosuperior spine. With this clip as a guide the x-ray tube is centered over a point one and one-half inches lateral and distal to the clip. In taking the lateral view the tube is in of the portable x-ray machine is placed at a level with the top of the table on the opposite side of the table from the fractured hip at the level of the knees. The well leg is then raised and held with the knee bent and the tube is focused obliquely at the fractured hip. A loaded cassette is then dropped into a sterile pillow clip held by the surgeon or an assistant, and the cassette is then held firmly against the body just under the costal margin with one edge of the cassette resting on the table and facing the hip joint at an angle of about 45 degrees to the long axis of the patient. In this position the x-ray film is exposed and gives an excellent lateral view of the head and neck of the femur.

A short incision is made through the skin and subcutaneous tissue in the lateral surface of the thigh extending downward from a point just below the greater trochanter down to the femoral condyle through the late l.

described. The distance drilled is estimated from measurement of the neck of the femur remembering the distortion caused by the distance of the femur from the x-ray film as well as the focal distance of the tube.

X-ray views are then taken in both anteroposterior and lateral planes to ascertain the correctness of the position of the guide pin or drill. If correct the pin or drill is removed and the length of screw required is more accurately determined by measuring the length of the pin that had penetrated the bone and then figuring from the x-ray picture the additional length needed. A starting tap having the same thread as the screw is then used through the cortex where the pin or drill was inserted, in order to permit the wide threads of the lag screw to traverse the cortex without drilling a hole larger than the shaft of the screw. The lag screw is then inserted and screwed into place in the direction found correct by the x-ray films when the guide pin was inserted. As the threaded portion of lag screw passes from the soft cancellous bone into the firmer bone structure near the cortex of the head of the femur the screw can be felt to grip into the bone as the fragments are thus drawn snugly together. With the lag screw in place another set of roentgenograms are taken, again in both anteroposterior and lateral planes, and while waiting for the report the incision is closed in layers. Should the x-ray view by chance reveal a misdirection of

the screw it is only a matter of seconds to remove sutures already placed and time is saved if the picture reveals satisfactory placement of the screw.

The entire procedure seldom requires more than thirty to forty five minutes, and the patient suffers little or no shock. The patient is returned to bed and the leg placed on pillows with the knee slightly flexed and the thigh moderately abducted. No splint, sandbag or other immobilizing equipment is necessary. Routine care is given and high back rest permitted as soon as tolerated. The patient is completely ambulatory in bed, and permitted up in a chair in two or three days. Walking with crutches is encouraged as soon as the patient is strong enough to use them, putting the affected leg down on the floor while walking but cautioned not to put any appreciable weight on it for two months. I have had several cases, however, where this advice was disregarded and walking without any crutches was resumed within a few weeks of the fixation and with no ill effects.

Postoperatively these patients are quite comfortable and have very little pain. They are able to eat and sleep, sit up on back, sit or lie on the well side and move around in bed. In the presence of a complicating arthritis they exhibit considerable pain, but this is probably due to the fracture trauma and the manipulations of the fracture reduction rather than the fixation. Pain continuing more than two or three days should be carefully checked for complications, such as arthritis, or destruction of the blood supply of the proximal fragment with swelling and beginning necrosis.

#### CONCLUSIONS

I have found this lag screw equally efficacious in intertrochanteric as well as intra capsular type of fracture utilizing the mechanical principle for which it was originally designed. In adapting it to the fixation of hip fractures, the fact that simplicity of insertion secures in the mechanical immobility of fragments, and a practical one piece screw that can be used by any surgeon without extensive equipment justifies its use and demonstrates its efficiency.

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## EPIDERMOID CYST OF THE SPLEEN

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THE recent observation of an epidermoid cyst of the spleen has prompted us to report the case and to consider briefly nonparasitic cysts of the spleen in general.

In 1829 Andral recorded the first case, presumably a dermoid. From then through June, 1946, the case has been reported 163 times. In a search of the available literature 15 (9 per cent) of the 163 cases have been reported as epidermoid.

The etiology of nonparasitic cyst of the spleen is not known. Various theories have been offered, including those of metaplasia of endothelium, herniation of splenic tissue, pre-existing lymphangiomas,<sup>1</sup> infarction or hemorrhage associated with pregnancy, menstruation, trauma, malaria, syphilis, tuberculosis, rupture of an intrasplenic artery or infarction due to arterial degeneration, misplacement of the William body<sup>2</sup> and of uterine horns.<sup>3</sup> We can add nothing concerning their etiology.

Of several classifications of splenic cysts proposed, that of McClure and Altmeppen<sup>4</sup> modified from those of Minahan<sup>5</sup> and of Fowler<sup>6</sup> is the most comprehensive as follows:

### I. True Cysts

#### A. Epithelial

1. Dermoid
- Epidermoid

#### B. Endothelial

1. Lymphangioma
- Hemangioma
3. Polycystic disease
4. Simple serous cysts

#### C. Parasitic

1. Hydatid echinococcus

### II. False Cysts

#### A. Hemorrhagic

#### B. Serous

#### C. Inflammatory

1. Acute necrosis in infection
2. Chronic tuberculosis

#### D. Degenerative liquefaction of infarcted area caused by embolism or arterial thrombosis

The symptoms and signs of nonparasitic splenic cyst vary depending on the size of the tumor and on the presence or absence of adhesions. Roentgenographic studies may be of diagnostic value. Because of the lack of any characteristic clinical picture and of the rarity of the condition the pre-operative diagnosis has been made very seldom.



FIG. 1

Fig. 1.—The superior surface of the spleen after it is removed.

Fig. 2.—The cross section of the spleen showing the enormous epidermoid cyst occupying the major portion of the organ, and a small daughter cyst at the extreme left. The resemblance of this and other published photographs of similar cysts is striking.

The treatment of choice is splenectomy. This has been accomplished with a low mortality (4 per cent). In those patients surviving no late complication has been recorded.

Our case of epidermoid cyst of the spleen appears similar to the cases of Poble,<sup>11</sup> Schneider,<sup>12</sup> Dinand (Iuharsch),<sup>13</sup> Santy, Shawan, Harding, Weil, Fremama, and Roux-Berge,<sup>14</sup> Gosset, Bertrand,<sup>15</sup> and Gosset, Lereboullet and

associates<sup>20</sup> and to the first case reported by Montgomery McNery and Frank.<sup>21</sup> In addition, Custer<sup>22</sup> reported five cases in a series of 5000 autopsies.

A description of the patient observed by us, treated successfully by splenectomy is recorded here.

Fig. 1

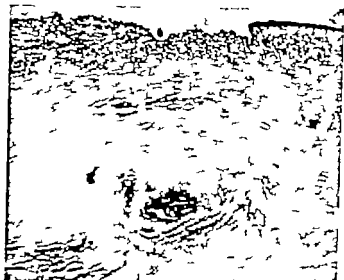


Fig.

the lining of the large cyst shows dense cellular reaction. At the junction of its epithelial lining the lining of the large cyst shows stratified

CASE REPORT (Roper Hospital No. 49034)—E. F., Negro female, aged 16 years, was admitted for the third time Aug. 12, 1946, because of manic depressive psychosis.

A very large mass, as found in the left upper quadrant of the abdomen. Its duration could not be ascertained. On the first admission, May 4, 1946, while pregnant she complained of epigastric pain and vomiting. No specific cause was found. Recovery was spontaneous. No mass other than the large uterus as noted. In an x-ray view of the abdomen the spleen not outlined. On the second admission, June 15, 1946, she gave birth to a premature male infant, her first child. The postpartum was unremarkable. The presence or absence of an abdominal mass other than the uterus was not recorded. After her return home, the patient continued to have the third admission.



Fig. 8.—A photomicrograph (x180) of the small daughter cyst shows a capsule and lining similar to that of the large cyst.

On physical examination, temperature, pulse, and respirations are normal. Blood pressure is 110/75. There were no abnormal findings except on mental and bilateral examination. She was mentally deranged. The abdomen was asymmetrical. A large bulging mass presented in left upper quadrant, extending three fingerbreadths below the costal margin. It was smooth, firm, freely movable and nontender. No notch was palpable. It projected from beneath the left costal margin. Its shape was constant with that of an enlarged spleen. The remainder of the abdomen was normal.

Necessary examinations included the following: red blood cell 3,400,000; hemoglobin, 10 Gm.; white blood cells 3,200. Differential, hematocrit, albumin, bleeding and clotting times, fragility test, platelet counts, skeletal bone marrow, sickle cell preparations, sedimentation rate, and serum index are all normal. Blood smears for malarial parasites are negative. Urinal and stool examinations are normal. Blood Wassermann and Elms test are negative. Intravenous pyelograms and gastrointestinal series are normal except for downward displacement of the left kidney and medial displacement of the stomach.

Laparotomy advised because of splenomegaly of unknown etiology. Malheur considered the most likely diagnosis.

On Sept. 7, 1946, under ether anesthesia, laparotomy was performed through left upper paramedian incision. The peritoneal cavity was free of adhesions. Immediately posterior to the large fluctuant mass measuring 30 by 13 by 13 cm. in diameter. There were

no adhesions about it. Most of the presenting surface was discolored but within this area there were patches which appeared gray and semitranslucent. Because of its size it was impractical to remove it intact. Thick, chocolate-colored colorless fluid, 2,000 cc. was separated. The fluid contained many short fine hairs, and small shimmering crystalline bodies resembling cholesterol crystal. Following this, the spleen was removed after ligation of its pedicle with silk ligatures. All other abdominal organs appeared normal. The wound closed in layers, without drainage with interrupted fine silk sutures. Immediately before and during operation, 1,500 cc. of citrated blood were given although there was no rapid loss of blood.

Bacteriologic and parasitologic studies on the fluid were negative.

On gross pathologic examination, the spleen was found to be soft and flabby (Fig. 1). On section, it was largely occupied by a cystic cavity measuring 12 by 10 by 11 cm. (Fig. 2) still containing 800 to 900 cc. of similar fluid. Adjacent to this was a small multilocular cyst 4 cm. in diameter. The wall of the large cyst was 4 mm. in thickness, tough and fibrous. At one end of the cyst there was a small amount of grossly normal splenic tissue. On microscopic examination, the cyst wall (Fig. 3) was thick and collagenous fibrous, showing variable numbers of inflammatory cells, foci of calcification, and many macrophages. The lining of the cyst wall was preserved in many areas, and consisted of stratified squamous epithelium showing keratinization and prickle cell formation (Fig. 4). Sections of the small cyst (Fig. 5) showed, in addition, a well defined basal layer of its epithelial lining. No hair follicles or other skin appendages could be found in numerous sections.

There were no postoperative complications. The wound healed per primam. Her mental state showed no change. She was discharged from the hospital on Sept. 18, 1946. On Feb. 17, 1947, follow-up report from mental hospital reported no later complications.

**Comment.**—At operation, it was felt that the cyst was a dermoid because hairs were present in the fluid. However, lacking microscopic proof the cyst is classified as epidermoid rather than dermoid.

#### SUMMARY

1. A brief review of the etiology, pathology, symptoms, and signs of nonparasitic cyst of spleen is presented.

2. Among 163 cases of nonparasitic cyst of the spleen previously reported, 11 cases (9 per cent) have been classified as epidermoid.

3. An additional case of an epidermoid cyst of the spleen, treated successfully by splenectomy is reported.

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# SCIATICA CAUSED BY CYST FORMATION IN OLD HEMATOMA

## REPORT ON THREE PATIENTS TREATED SURGICALLY

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**A**MONG the patient who have consulted me because of severe back pain owing to fascial fat hernias were three women who had, in addition, unusual manifestations of sciatica which could not be attributed to the fascial fat herniations causing the more generalized back pain. In all three, the pain radiated down the leg, and was more severe when the patient was sitting; one patient (Case 3) also complained of discomfort on walking and displayed an abnormal gait. The sciatic symptoms in all these cases were apparently initiated by trauma, and in all three removal of a fibrous cyst in the region of the sciatic nerve relieved the pain.

In view of the striking similarity in the history, symptoms, and physical findings in these cases—especially since all of the patients had fascial fat hernia as well as the fibrous cyst in obliterating the sciatic nerve—it would seem of interest to report them as a group.

### CASE REPORTS

**CASE 1**—A woman, aged 41 years, had suffered for ten years from severe backache which more intense right side had distal trigger point of pain in the back for years but the pain did not radiate to the legs. She consulted some different physicians, he treated her for arthritis, but she obtained no relief. One evening I examined her who had had several severe falls, which greatly aggravated the symptoms. About six months before she began to notice pain on sitting, which referred to the buttock, and down the left thigh and leg, and had increased steadily. At the time this pain was noted, the patient had also developed a tumor on the buttock. She had continued to seek relief from the suffering, but all treatment had been ineffective. At the time she consulted me, she had been advised not to see any further about her physical condition had come to the conclusion that the difficulty was permanent.

Physical examination of the back and legs. The fourth and fifth lumbar vertebrae and trigger point of pain in the left sacral region, which was relieved by repeated injections of anesthetic solution. There was also a large palpable mass in the left buttock. The area also injected with anesthetic solution. The first injection relieved the pain, but was not successful, but a deeper injection of larger amounts of anesthetic solution, the patient obtained temporary relief from the pain in the leg. The preoperative diagnosis was fascial fat hernia in the left sacral region and lipoma of the left buttock.

At operation, herniated fat was visible over the left sacral region, and a large mass of dense fibrous tissue which extended through an incision over the left buttock. The patient experienced relief both from the back pain and the pain down the leg.

Post-operative examination six weeks later, and was still entirely symptom free.

**Pathological Report**—The mass of herniated fat showed mature hemoglobin fat supported by strands of dense fibrous connective tissue. Sections of the tissue removed from the buttock showed that the fat was all composed of mature adipose cells, from connective tissue, richly vascularized with capillaries and arterioles. Focal areas of degenerative change with swelling and necrosis of the fat cells were present in several areas along the periphery of the mass of lipoma. The inner aspect of the cyst was

generally detached lining except focally for pseudoepithelial covering apparently consisting of mesenchymal cells attached to the inner aspect of fibrous and small fragments of blood clot (Fig 1).

The pathologic diagnosis was dense tissue and fibrous yet the seat of chronic inflammation.

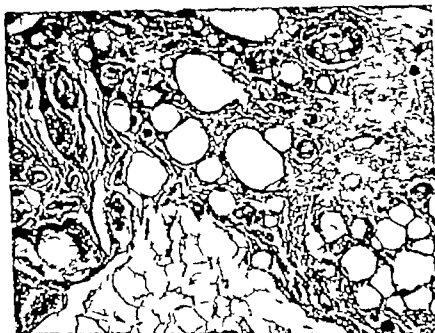


Fig 1 (C x 100) — cell some consist of fibrous and thickly sacculated with capillaries and small blood vessels. The lining is composed of pseudoepithelial cells and polymorphonuclear leukocytes. Some of the cells are in places.

CASE — A woman, aged 33 years, was examined in February 1947. She had suffered an injury to the left knee in 1935. She had continuing pain and had the typical history of the growth of relief from arthroplasty, including arthroscopy and from arthroplasty. The pain on the left side of the knee was more severe than the patient sitting, and when she was all down the thigh and leg. The pain also aggravated the movement of the leg especially on flexion of the left leg and on flexion of the right thigh on the bed.

The physical examination was revealed tenderness over the left medial joint. There was no swelling and no pain on palpation of the knee, and relief of the pain by injection of anesthetic solution. Deep palpation also revealed some tenderness on the left buttock, both of which were related to injection of anesthetic solution. The preoperative diagnosis was multiple hematomas of trauma.

At operation, several fragments of bone were excised from the left medial region. After hemostasis, a large mass was removed from the left buttock. It consisted of a removed and also cyst containing a fluid which was filled with fluid.

The pathologic diagnosis was dense tissue and fibrous with extensive hemorrhage and cellular infiltration.

Operation relieved the pain on the left knee and leg, and six months afterward the patient was examined and found to be asymptomatic.

CASE 3—A woman, aged 48 years, had had severe pain, leading on her back, three years before I first examined her. Several subfascial fat herniations are found and excised, but this operation afforded little relief. The back remained tender and the patient complained of difficulty on walking, and of more severe pain when sitting.

Physical examination showed marked tenderness over the cervical, upper thoracic, middle lumbar and sacral regions. The patient complained that the pain was aggravated when she was sitting. She walked with the right foot everted. In view of the similarity of symptoms in this and the first preceding case, an attempt was made to palpate over the buttock, but none was found. Nevertheless, injection of anesthetic solution in the right sacral region afforded some relief from the pain in the leg.

A neurologist who saw her in consultation suggested exploration of the right sacral region. This was done with removal of cyst, 6 by 14 cm. from this area. When the thigh was flexed during the exploration, fluid was forced out from the lower end of the cyst.



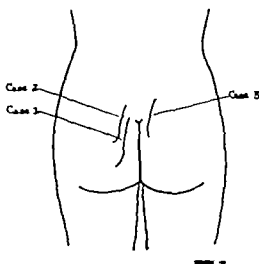
Fig. 2 (Case 3).—Cyst, all composed of dense fibrous tissue, no granulation tissue. The latter occurs adjacent to the lower aspect which shows adherent masses of fibrin and blood clot. There is diffuse lymphocytic infiltrate.

Microscopic examination showed fibrous cyst and fibroepithelial tissue the seat of chronic inflammation (Fig. 2).

When the patient was examined three months after operation, she had no discomfort on sitting, and the gait was normal. The pain in the thigh and leg had disappeared.

Sclatosis, a term first used by Cotugno in 1784, has been applied to any condition characterized by pain in the lower part of the back and the lower extremities, regardless of cause, giving clinical manifestations. It is a general term which has included neuralgia, neuralgia parasthetica, neuritis, radiculitis, protruded intervertebral disk, myalgia and myositis.

The spinal cord terminates opposite the first lumbar vertebra. The nerve roots forming the cauda equina arise from the lumbar and sacral regions of the spinal cord, descend in the subarachnoid space intradurally and are freely movable except as they approach their exits. At the level of the sciatic notch, all these components unite to form one band—the sciatic nerve. The nerve passes around the ischial spine and descends in the posterior portion of the buttock between the ischium and greater trochanter. The piriform muscle bridges the widest portion of the nerve and occasionally is split by the components of the nerve. The gluteus maximus covers the nerve below this point. The nerve then descends in the posterior part of the thigh into the interspace between the semitendinosus and semimembranosus medially and the deep femoris laterally.



71 —Illustrate pharmacological actions of certain drugs causing acid-base symptoms

Pathologic changes affecting the sciatic nerve are principally those of pressure neuritis, and the intervertebral foramen constitutes a critical region for symptoms arising from this cause. Chronic sciatic pain is usually caused by pressure or irritation of the sciatic nerve from an external source. According to Lewis, predisposing factors are congenital anomalies, circulatory or endocrine disturbances, and trauma.

In the three cases reported here in which pressure on the sciatic nerve was caused by a fibrous cyst in the buttock, it would appear that the original cause was trauma, since all the patients had a history of injury preceding the

Many of the articles submitted for publication have found their way into the fourth case book. The articles were made by the staff of the FBI, the chief counsel was the one who submitted them. The examination revealed the results of the fifth month's work. The per cent of the last solution.

onset of symptoms. In two cases, the cystic mass was palpable but in the other it was discovered by exploration although suspected preoperatively on the basis of the striking similarity of symptoms to those in the first two cases.

In the first two cases, the cystic mass was in the left buttock and in the third, on the right. In none of these instances was the sciatic nerve itself involved in the lesion. The situations of the lesions varied (Fig. 3) but in all they were close to the sciatic nerve so that, with certain movements, the nerve was subjected to abnormal pressure producing severe pain. In the first two cases, it seems evident that the pain experienced by the patients in the sitting position was caused by direct pressure on the sciatic nerve. In the third case, the cyst was elongated and the large quantity of fluid it contained shifted with motion. It is presumed that in this instance the pressure of this shifting fluid content produced the pain.

#### SUMMARY AND CONCLUSIONS

Three cases of lesions apparently initiated by trauma, are reported.

Surgical exploration in each of these cases disclosed a hematoma with cyst formation.

All three patients were relieved of the severe radiating, sciatic pain by excision of the cyst.

These findings may be significant in certain cases of sciatica in which other causes of pain have been eliminated.

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## AMPUTATION OF THE CANINE ATRIAL APPENDAGES

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THROMBUS formation in the left atrial appendage is a frequent sequela of rheumatic mitral disease, and subsequent repeated arterial embolism often produces disabling or fatal complication. There are no effective methods to prevent such thrombus accretion or embolization therefrom. The use of the anticoagulant drugs, heparin and dicumarol, offers one possible solution of this problem. It has seemed to us, however, that in selected cases of repeated embolism a more direct approach might be feasible, namely, surgical excision of the thrombus-containing atrial appendage. As a preliminary step, the following experiments were performed to determine the effect of amputation of one or both atrial appendages of normal dogs.

### METHODS

Experience and confidence in this type of cardiac surgery were obtained in a series of previous experiments where through the same approach, broad flaps of myocardium were elevated on each side of the descending coronary artery branches and sutured back on the chest. This was done in an attempt to produce heart failure in the dog by thinning the effectively functioning myocardium.

In the excision of the atrial appendages eight dogs were used, each weighing between 8 and 11 kilograms. Food was withheld for twenty-four hours prior to surgery. Under intravenous pentobarbital sodium anesthesia (— mg. per kilogram) the animal was placed in the right lateral position and a skin incision made in the fifth or sixth left intercostal space. The incision was three to four inches long, running parallel to the ribs and extending from the left parasternal line to the left anterior axillary line. The incision was carried down to the parietal pleura, and as soon as the pleural cavity was entered mechanical artificial respiration was instituted and maintained throughout the remainder of the operation until the pleural cavity was closed. In the first few animals, portions of the fifth or sixth left ribs were resected. Subsequently it was found that adequate exposure could be obtained by retraction of the ribs without rib resection. Following entrance into the pleural cavity the left lung was retracted and protected with a towel moistened with isotonic saline solution. The left atrial appendage was easily seen through the parietal pericardium. The left atrium was incised longitudinally parallel to the left phrenic nerve over the base of the appendage. One to two cubic centimeters of 20 per cent solution of procaine were applied topically to the atrial appendage to abolish the atrial rhythm. In some cases, procaine was injected directly into the atrial myocardium in the region of subsequent amputation. An Allis clamp was then placed on the tip

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of the atrial appendage and a right angle clamp or curved hemostat clamped across the base of the appendage. In two dogs, two transfixion sutures were placed below the clamp and tied securely. In the remainder of the dogs, simple ligation at the base of the appendage sufficed. The atrial appendage was then amputated with scissors, and a transfixion suture was placed as reinforcement distal to the encircling ligature. Atraumatic needles and 00 catgut or braided silk sutures were used. There was no significant bleeding. The parietal pericardium was incompletely closed with interrupted silk sutures, leaving a 1 cm. aperture in the base of the pericardial sac allowing drainage into the pleural cavity. The parietal pleura was closed, artificial respiration discontinued, and the chest wall repaired in the usual manner. After closure of the chest, residual air was aspirated by needle and syringe. Intravenous papaverine (15 mg.) was used in some cases to stimulate spontaneous respiration when artificial respiration was discontinued.

Exactly the same operative procedure was followed when the right atrial appendage was excised, except that the animal was rotated to the left lateral position after the pericardial cavity had been entered. In five animals, the left atrial appendage in two the right atrial appendage, and in one both atrial appendages were removed.

Postoperatively the animals were placed in individual cages, and 200,000 units of penicillin were administered intramuscularly daily for ten days. Serial electrocardiograms (three standard limb leads, and precordial leads from the apex and the third right parasternal intercostal space using the right foreleg or central terminal as the location for the indifferent electrode) were taken preoperatively, immediately after surgery, two weeks following surgery, and before sacrificing the animals, four to twelve weeks following the operation.

#### RESULTS

Seven of the eight dogs survived the operation. The first animal developed respiratory difficulty, and the heart ceased beating 15 minutes after chest closure. The other seven dogs had an uneventful postoperative course. Within twenty-four hours after surgery they were ambulatory and eating well, and within one week they were lively and behaved as did nonoperated dogs.

The serial electrocardiograms did not reveal any abnormal atrial rhythms. The P and T deflections varied somewhat in direction and amplitude from record to record. These variations are ascribable to changes in position of the animal and its heart. Although an attempt was made to keep the animal in the same position each time a record was taken, there were no abnormal deviations of the S-T-T or P-T segments which would indicate significant injury to the ventricles or atrial myocardium. One animal developed a broad, notched P wave in Lead II immediately following surgery, indicating intra-atrial block. This abnormality had disappeared by the time the subsequent electrocardiograms were made. The P-R interval remained unchanged in all animals.

Two dogs were sacrificed four weeks postoperatively; the remaining animals after twelve weeks. Necropsy revealed firm adhesions between the visceral and

parietal pericardium, only in the region of the stump of the atrial appendage. Elsewhere the pericardium was smooth and glistening. In the dogs in which both atrial appendages were removed, there were thin, fibrous pleuropericardial adhesions in the region of the incision of the pericardial sac. The atrial incisions were firmly healed in all dogs, and the endocardial surface was well endothelialized. There were no dilatations in the region of the amputation stump or adherent mural thrombi (Fig 1). Careful examination of all organs failed to reveal congestion, emboli, or infarction. Sections were made through the atrial amputation stump and stained with iron hematoxylin and eosin, trichrome and the

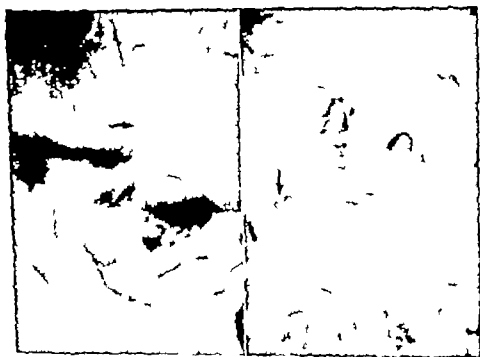


Fig 1.—A Photomicrograph of endocardial surface of atrial amputation stump showing suture line. B Higher magnification of endocardial surface showing endothelial lining and layers of myocardium (arrows).

van Gieson stain for late tissue (Fig 2). The following report was made: There was severe fibrosis along the line of suture with formation of cellular connective tissue irregularly disposed and the ventricle of hyperplastic endothelium of cells—large polygonal morphonuclear leucocytes, and some plasma cells. This extended through the muscular coat and the endocardium and in old of the endothelial lining the latter showed a mural thrombus, and was re-endothelialized. In the ventricle of the ligatures there was fibroblastic hyperplasia and formation of small vascular granulation tissue showing dense cellular



infiltrate. There were occasional foreign body giant cells, and also a moderate number of monocytes containing iron pigment. There were no abscesses. In general the degree of inflammation was not severe.



Fig. 2.—Vas Gieson elastic stain of section through apex of atrial appendage five weeks after operation (x4). A, endocardial surface showing border of suture; B, remnant of lumen; C, external surface; D, extension of fibrous along line of suture.

#### COMMENTS

The atrial appendages serve no significant function and their removal should not compromise the cardiovascular system. Amputation of one or both atrial appendages was successfully performed without subsequent mural thrombosis, embolism, persistent disturbances of rhythm, or congestive heart failure. The atria healed readily to produce a firm, well-endothelialized scar and the myocardium united in a firm manner in a logically similar to that of muscle wounds elsewhere in the body. Beck and others<sup>1</sup> have repeatedly emphasized the property of primary healing of wound of the heart and the tolerance of both human and canine hearts to trauma.

We recognize the fallacy of transposing unreservedly the results of surgery on the heart of the healthy dog to the diseased heart of man. Moreover the healing capacity of the dog differs considerably from that of man. However, the further consideration of the effects of surgery on the heart with rheumatic heart disease and mitral stenosis, the more we are inclined to believe that the atrial appendages may be manipulated or excised also suggests that the atrial approach or used in surgical procedures on the mitral valve rather than the direct ventricular approach as has been used principally in the past.

# SUMMARY AND CONCLUSIONS

1 Seven of eight dogs survived unilateral or bilateral atrial appendectomy. One dog died immediately after the completion of the operation. The postoperative course was essentially uneventful in all surviving dogs. Serial electrocardiograms failed to reveal abnormal atrial rhythms or evidence of atrial injury except in one dog who developed transient intra-atrial block. Necropsy revealed excellent healing with a firm scar which was well endothelialized without adjacent mural thrombosis. Localized pericardial and pleuropericardial adhesions were found in the region of the amputation stump.

2 Excision of one or both atrial appendages is feasible in dogs.

3 It is suggested that clinical applications of this method be given further consideration.

4 The left atrial appendage approach for surgery or dilatation of the mitral valve is suggested in preference to the ventricular approach.

We are indebted to Dr. L. N. Katz for his criticisms.

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## THE TREATMENT OF MALIGNANT LIP FURUNCLES WITH EMETINE

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THE common type of *furuncle* is usually defined as a circumscribed perifollicular suppuration followed by massive necrosis of the central hair follicle together with its sebaceous glands. When a similar process befalls not single follicle but a continuous group of them the term *carbuncle* is generally used. Such a differentiation is, as I have pointed out over a long period, far from being correct. In the first place many typical furuncles are so voluminous in densely haired parts, as on the head that for the process to occur in single follicle is not possible. In reality the characteristic feature of a carbuncle consists in the formation of military abscesses in its periphery under continuous dissemination of these miniature foci the carbuncular structure enlarges. The question how these military abscesses develop themselves cannot yet be answered in a satisfactory manner. Nevertheless, it is important to know that their spreading is not limited to the skin and the subcutaneous tissues but they may also involve deeper layers. Therefore in advanced cases of neck carbuncles these military abscesses can infiltrate the underlying muscles. As satellites of malignant furuncle of the lip they make their appearance in the submucosa and the mimetic muscles. Even in metastatic manifestations, which often follow this type of staphylococcal infection, the same groupwise formation of military abscesses can be encountered. The so-called metastatic carbuncle of the kidney is its classic representative. In any rate it is a question of mere convenience for this special type of progressive purulent infiltration in the proximity of a furuncular structure to be called carbuncle or malignant furuncle. It is astonishing that this typical anatomic feature which I first described in 1931, and which can easily be verified when a carbuncle or malignant furuncle is thoroughly opened in due time is not even mentioned in the current textbook. Only in late cases, when the military abscesses have melted into large purulent tracts, the primary characteristic structure finally becomes unrecognizable.

The tendency to septic generalization is especially high in malignant lip furuncles. The rapid involvement of the adjacent veins—in the first place the vena angularis, with the well known fatal consequences for the virus carriers—and the leptomeninges—mostly responsible for it. Nevertheless, the development of septicemia is not necessarily bound to the competition of thrombophlebitis. When the initial furuncle once has assumed a malignant character—recognizable by the onset of fever often accompanied by chills and a quickly progressing and considerable swelling of the lip as well as pain, rapid deterioration of the general conditions—the chances of recovery are generally poor.

In the past, operative treatment has generally been regarded as indispensable in severe cases. However for more than thirty years conservative

measures have been considered nearly everywhere as more promising. A short historical exposure on this behalf is to be found in my paper of 1906.<sup>1</sup> Typical of this predominant conservative tendency might be considered the formulation of *Ch. Lecomant*. The confinement to conservative measures helps the organism to limit the infection. My own experiences led me to quite different conclusions. In my previously mentioned article I attempted to explain that nonoperative procedure can be useful only in rather benign cases, whereas in the presence of real malignant development a positive result if obtainable at all, can be expected only from a large débridement of the infected area combined with section of the angular vein. This latter is done by a transverse incision made 1 to 2 cm. beneath the interior angle of the orbita, dividing the soft parts down to the bone. For many years I have employed this method with fairly good results. However I have since found out that emetine can be a precious drug against various septic conditions and this led me to try it also against malignant furuncles. The result I obtained were so satisfactory that the last cases operative measures could be entirely omitted. Before entering on the details of these experiments some previous explanation of this new use of emetine will be necessary.

Emetine the well-known alkaloid of the *Ipecacuanha* has been used for surgical purposes as an often successful drug against tropical liver abscesses due to amebic infection. Furthermore it has been used occasionally against lung abscesses, and if a positive result occurs this has often been regarded as sufficient proof for the amebic nature of the suppuration. The good results I obtained in Ankara in cases of liver abscesses which had no relation to previous amebic disorders made me doubt the exclusive antiamebic efficiency of emetine and further experiences gave clear evidence that this drug can be very useful in many non-specific infections. Especially good results were obtained in severe cases of peritonitis of different origin (appendicitis or traumatic lesions of the bowel) in severe biliary infections, in general septicemia and in gaseous gangren. In many of these cases emetine acted as an important supplement to surgical procedure but sometimes no other treatment was needed.

The theory of this new therapeutic capability of emetine has still to be developed. The new instantaneous effect which often can be seen under these conditions is its most striking feature and could point to the assumption of a high antiseptic efficiency. It cannot be regarded as a mere bacteriostatic one as will be explained later. This is supported by experiments made in vitro by P. Berionelli. Again in vivo that is, in infected animals, this author entirely confirmed my clinical experiences.

In eight cases of malignant furuncles of the face to date I have used emetine—partly alone partly as a supplement to failing surgical procedure. To give an idea of its efficiency a short report of these cases is indispensable.

#### CASE REPORTS

Case 1 (Prod. N. 133).—A man 30 years of age entered the hospital Sept. 27, 1913, with a malignant furuncle of the upper lip which began four days previously. He had had

several chills and the temperature was 39° C. A large incision was made. In the afternoon the temperature rose, accompanied by a new chill, to 39.5° C; the following morning the temperature was 39.5° C. The pusculence in the incision persisted and the general state became alarming. Emetine (0.63 Gm per day) was given. As Fig 1 shows, this was followed by a rapid fall of temperature. Such became normal in the course of few days. Still more striking was the change in general condition, which became very satisfactory almost immediately afterward. Rapid diminution of the local swelling and the other inflammatory signs followed. The patient was discharged from the hospital completely recovered after ten days.

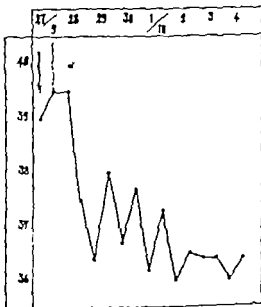


Fig. 1

CASE 1.—Orbit, 1. Case of age admitted to another service in 1945. On February 2, a rise of the lower lip had made it necessary to treat the rapid increase of the local swelling together with the general state. The patient was treated with emetine (0.63 Gm per day) and a large incision was made in the infiltrated area as usual, but with a temporary limitation of the fever was obtained, whereas the local swelling showed considerable increase. The general state was also alarming. Albuminuria 0.5 per cent. On February 13, the fever became very enlarged, the angula was also (no noble thrombosis) and emetine 0.63 Gm per day (on February 19) administered. This was followed by a brief decrease and rapid disappearance of the fever. Also, the local condition and the general state showed quick improvement. The patient was discharged home on March 2, as practically cured. The rise there still trace of albumin. A short time afterward the recovery was complete.

CASE 2 (Prot. N. 41.1).—Loret 74 years of age admitted April 17 1945, with malocclusion of the upper lip. The affection had developed in the course of three days. The lip showed a enormous smooth swelling and the malocclusion marked nearly the lower angle of the orbit. The general condition was serious. With repeated attempts I opened the left side of the upper lip with a large frontal incision and it was found that all strands were crimped by a very narrow section of the angular vein was done.

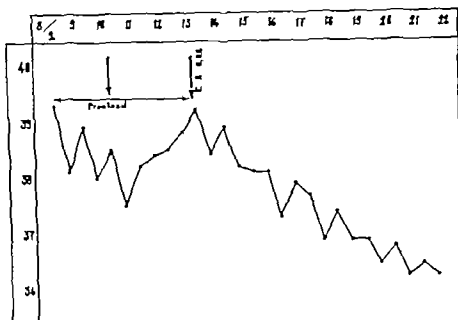


Fig. 2

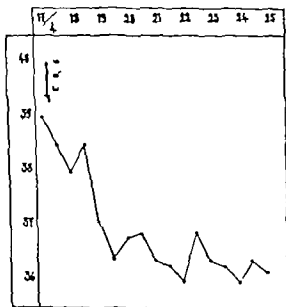


Fig. 3

and simultaneously emetine as given (0.06 Gm per day) and continued up to April 23 (0.42 Gm. in all). The following day the patient felt well the swelling as quickly decreasing. From April 20 he was definitely without fever (Fig. 3) and was discharged as cured on April 25.

CASE 4 (Prot. No. 11953)—Female, 22 years of age as admitted Oct. 21 1914, with malignant furuncle of the upper lip of five days duration. There was pain, fever and insomnia. At the time of admission, the whole lip showed knotlike swelling and the left cheek was also involved. Since the temperature was not very high (Fig. 4) with absence of chills, the treatment in the first days was only symptomatic. On October 21, the swelling showed considerable increase and emetine was given (0.03 Gm twice daily continued till October 29 0.42 Gm total). As early as the following day the patient declared that for the first time she had slept well the pain was entirely gone. Subsequently the infiltration diminished quickly and the general state as perfect. The temperature as normal from November 7. On the following day small superficial incision developed in the region of the neck without any thrombosis reaction. On November 12 the focus as opened. The pus contained *Staphylococcus aureus*. Only three days the small wound healed. The patient was discharged as cured November 14.

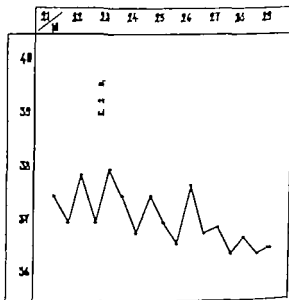


Fig.

CASE 5 (Prot. N. 12930)—Male 18 years of age, as admitted Oct. 9, 1917, with furuncle of the upper lip of three days duration. There as growing pain and swelling. Several times there was feeling of shivering but not real chill. This was typical malignant furuncle with large surrounding edematous swelling. The general state was not severely altered, and the temperature was only 37.4 C with 17,500 leucocytes per cubic millimeter in the blood. Emetine (0.03 Gm twice daily) as given. The following day the patient felt better. The second day the temperature as normal, and the swelling diminished. On October 11 some pus as evacuated by spontaneous perforation of the skin. On October 13 the leucocytes were diminished to 9,400 per cubic millimeter. The patient was discharged from the hospital cured on Oct. 15.

CASE 6 (Prot. N 13094) — 11 km, 22 years of age was admitted to the hospital Oct 11 1947 with furuncle of the lower lip. There was considerable edema on the general feeling of malaise and severe pain with leucocytosis. The temperature was 37.5 C. Emaline (0.03 Gm. twice daily) was given. The treatment was followed by immediate relief of pain and quick diminution of the swelling. The patient was able to sleep without the aid of narcotics. The temperature became normal on October 14. The leucocytes were 11,000 per cubic millimeter on October 13 and 8,900 on October 15. The patient was discharged on October 18.

CASE 7 (Prot. No. 7337) — Female, 18 years old, was admitted June 14 1947. A furuncle of the upper lip had begun a harmless abscess six days previously there was increase of the swelling and pain with strong headache, general bad feeling, and high fever. At the time of admission the temperature was 39.6 C. There was considerable swelling of the upper lip with involvement of the cheek extending to within the region of the orbit. The general condition was poor. Immediate medication with emaline was instituted (0.06 Gm. the first day 0.04 Gm. the following days, until June 21, total 0.60 Gm.). The changes which took place under this treatment are very striking. On the first day after emaline (Fig. 5) the temperature became practically normal. The patient declared spontaneously that very short time after the first injection she had wonderful feeling of well being. On June 17 the formerly large swelling was already reduced to the size of a small cherry spontaneous perforation followed and the patient discharged June 1 cured.

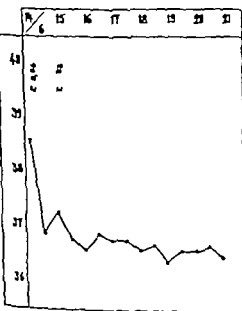


Fig. 4

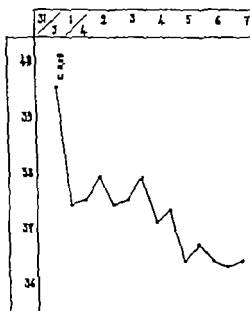


Fig. 5

CASE 8 (Prot. N 2334) — Ribet, 34 years of age, admitted March 21 1947. A malignant furuncle of the upper lip. In the previous ten days there had been ten violent attacks of pain transferred on the and he was under the grip of long lasting severe pain. There was a local abscess of the lip. The abscess had broken on the lip of the surrounding tissue. The temperature was 39.6 C. The rise contained trace of albumin and some erythrocytes. The blood count indicated the presence of leucocytosis. The patient received the first dose (0.04 Gm. emaline) was immediately given and the treatment was continued until April 7. 64 Gm. total. The following day



the temperature showed critical decline it became normal four days afterward (Fig. 1). There was no recurrence of chills and all other signs disappeared in short time. The patient discharged as cured on April 10.

These eight cases of malignant furuncle of the face represent the total of those patients treated with emetine and in every case a very satisfactory result was obtained. In a critical analysis of them it should be considered that their clinical importance is not a homogeneous one. Therefore in Cases 5 and 6 although belonging certainly to the class of malignant furuncles, the symptoms were mitigated. If the whole material had been of the same kind, it would be impossible to attribute the good final results with sufficient precision to the mere action of emetine. Similar doubts could be expressed for Case 3. Undoubtedly it was a very bad case but a large incision had been made and no one could deny the possibility that the recovery might have been due to the surgical procedure. As I have explained before, I have been fervently partial to the surgical treatment of malignant furuncles, because the results obtained were very satisfactory. But the recovery which followed the incision in Case 3 was more prompt and in every way more impressive than ever before when incision alone was made. The assumption seems justified, therefore, that a considerable part of this favorable reaction must be attributed to emetine.

But even the most intransigent critic will have to acknowledge the really amazing effect of emetine obvious in the other cases. Very significant is Case 1. The initial incision was followed by a new rise in temperature, accompanied by a chill and growing local swelling. It may be that the incision had not been made to sufficient extension. But nevertheless it is known that under those conditions the prognosis becomes very bad. In this situation the administration of emetine was immediately followed by an immediate amelioration and quick recovery. This dramatic change means more than a mere coincidence. The same was seen in Case 11. Here also, surgical intervention had been made before but things took a dangerous turn and the final recovery was certainly due more to emetine than to the completing of the primary incision. An equally rapid amelioration of highly critical conditions followed the administration of emetine in Cases 7 and 8. The most remarkable of them is undoubtedly Case 8. Not less than ten long-lasting chills had made their appearance in the last twenty-four hours in this patient and *leptospira* were as found in the blood. But this dangerous situation was entirely altered the following day. No chill recurred and final recovery took place in a short time. These last observations are so persuasive that no serious objection can be made against my interpretation. A further proof for this affirmation results from the fact that this reaction to emetine is not a phenomenon to be seen only in malignant furuncle. If emetine has any effect at all it is in the most severe form, namely in cases of generalized peritonitis, severe bilious infection, purulent traumatic meningitis, or gangrenous gangrene. In my former publications numerous examples of this kind of febrile reaction are to be found.

It might also be mentioned that sometimes the patient spontaneously indicates the feeling of restored comfort even before the objective signs are manifested. In Cases 4, 5, 6 and 7 such a sensation was noticed.

It was already mentioned that a sufficient theoretical explanation on this behalf is still lacking. Nevertheless, the effect of emetine is not a strictly bactericidal one. In patients with widespread peritonitis a favorable reaction to emetine does not exclude the possibility that harmless residual abscesses might make their appearance afterward. As sequelae of septicemia these mitigated suppurations can, for instance, develop at places where injections, even of emetine, had been made. A characteristic example for this is seen in Case 4 where a small abscess still containing staphylococcus followed the acute furuncular infection.

The dosage of emetine hydrochloride 1% for the adult, 0.03 Gm. twice daily up to 0.06 Gm. twice daily. Also when a full effect is obtained, the medication must be continued to the total amount of about 0.4 to 0.9 Gm. or even 1.0 Gm., for if interrupted too early recurrence of the infection can take place. When correct dosage is used, cardiovascular difficulties, as sometimes observed in dysentery cases, are not to be expected. In any case, the combination with a slightly stimulating drug might be recommended as a prophylactic measure.

#### CONCLUSION

Eight cases of malignant lip furuncles are reported. All of the patients recovered, mostly without any surgical interference, by mere use of emetine. The effect of the drug is generally a striking one. Even under the worst conditions, that is, when septicaemia is already present, quick and complete recovery can be obtained. Emetine, which has given similarly satisfactory results in numerous nonamebic septic infections of different types, can therefore be regarded as an important agent for the treatment of malignant lip furuncles.

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#### Erratum

In the article by Reynolds and Young, J. entitled "The Use of the Roux-Y Extender in the Operability of Carcinoma of the Stomach and of the Lower End of the Esophagus" in the August 1949 issue of the JOURNAL, the sentence beginning in the fourth line, page 400: "Whole blood administered at a rate of 1 lit. an hour" should read "at a rate of 1/2 liter an hour."

the temperature showed critical decline to become normal four days afterward (Fig. 6). There was no recurrence of chills and all other signs disappeared in short time. The patient was discharged cured on April 10.

These eight cases of malignant furuncle of the face represent the total of those patients treated with emetine, and in every one a very satisfactory result was obtained. In a critical analysis of them it should be considered that their clinical importance is not a homogeneous one. Therefore in Cases 3 and 6 although belonging certainly to the class of malignant furuncles, the symptoms were mitigated. If the whole material had been of the same kind, it would be impossible to attribute the good final result with sufficient precision to the mere action of emetine. Similar doubt could be expressed for Case 3. Undoubtedly it was a very bad case but a large incision had been made and no one could deny the possibility that the recovery might have been due to the surgical procedure. As I have explained before, I have been fervently partial to the surgical treatment of malignant furuncles, because the results obtained were very satisfactory. But the recovery which followed the incision in Case 3 was more prompt and in every way more impressive than ever before when incision alone was made. The assumption seems justified, therefore, that a considerable part of this favorable reaction must be attributed to emetine.

But even the most transient critic will have to acknowledge the really amazing effect of emetin obvious in the other cases. Very significant is Case 1. The initial incision was followed by a new rise in temperature accompanied by a chill and growing local swelling. It may be that the incision had not been made to a sufficient extension. But nevertheless it is known, that under those conditions the prognosis becomes very bad. In this situation the administration of emetine was immediately followed by an impressive amelioration and quick recovery. This dramatic change means more than a mere coincidence. The same was seen in Case 4. Here also surgical intervention had been made before but things took on alarming turn and the final recovery was certainly due more to emetin than to the completing of the primary incision. An equally rapid amelioration of highly critical condition followed the administration of emetine in Cases 7 and 8. The most remarkable of them is undoubtedly Case 8. Not less than ten long lasting chills had made their appearance in the last twenty-four hours, in this patient and 41 per cent were found in the blood. But this dangerous situation was entirely altered the following day. No chill recurred and final recovery took place in a short time. These last observations are so persuasive that serious objection can be made against my interpretation. A further proof of this affirmative result from the fact that this reaction to emetine is not phenomenon to be seen only in malignant furuncle. If emetin has an effect to all erythema associated in this dramatic form, may it be in cases of generalized peritonitis, severe bilious infection, purulent traumatic meningitis or gaseous gangrene. In my former publications numerous examples of this kind of fulminant reaction are to be found.

It might also be mentioned that sometimes the patient spontaneously indicates the feeling of restored comfort even before the objective signs are manifested. In Cases 4, 5, 6, and 7 such a sensation was noticed.

It was already mentioned that a sufficient theoretical explanation in this behalf is still lacking. Nevertheless the effect of emetine is not a strictly bactericidal one. In patients with widespread peritonitis a favorable reaction to emetine does not exclude the possibility that harmless residual abscesses might make their appearance afterward. As sequelae of septicemia those mitigated suppurations can, for instance, develop at places where injections, even of emetine had been made. A characteristic example for this is seen in Case 4 where a small abscess still containing staphylococcus followed the acute furuncular infection.

The dosage of emetine hydrochloride is, for the adult, 0.03 Gm. twice daily up to 0.06 Gm. twice daily. Also when a full effect is obtained the medication must be continued to the total amount of about 0.4 to 0.9 Gm. or even 1.0 Gm. for if interrupted too early recurrence of the infection can take place. When correct dosage is used, cardiovascular difficulties, as sometimes observed in dysentery cases, are not to be expected. In any case the combination with a slightly stimulating drug might be recommended as a prophylactic measure.

# CONCLUSION

Eight cases of malignant lip furuncles are reported. All of the patients recovered, mostly without any surgical interference by mere use of emetine. The effect of the drug is generally a striking one. Even under the worst conditions, that is when septicemia is already present, quick and complete recovery can be obtained. Emetine, which has given similar satisfactory results in numerous nonamebic septi-infections of different types, can therefore be regarded as an important agent for the treatment of malignant lip furuncles.

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# Erratum

In the article by Reynolds and  
and the Oj rated by J. Curran, of  
in the August, 1915 issue of the J.  
the Whole blood drawn after the  
in 1 1/2 liter hour

of 1 liter an hour should read

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## Case Reports

### ENDOBRONCHIAL POLYPOID HAMARTOCHONDROMA

#### REVIEW OF THE LITERATURE AND REPORT OF A CASE

R. W. POSTLETHWAIT, M.D., WINSTON-SALEM, N. C. AND R. F. HAGERTY, M.D.  
AND J. C. TRENT, M.D., DURHAM, N. C.

**E**NDOBRONCHIAL polypoid hamartochondromas are rare lesions comprising only a small portion of all hamartomas of the lung. Only thirteen cases of this type have been reported. They arise as a polypoid growth within the bronchial tree and are composed principally of cartilage, with or without fat, epithelium, or connective tissue. The clinical and therapeutic differences between endobronchial and intrapulmonary hamartochondromas are considerable. An intrapulmonary lesion may remain asymptomatic for years, and grow to considerable size before pressure may cause symptoms. A small endobronchial lesion, however, may cause severe symptoms early when of small size because of the resulting obstruction. Also, an intrapulmonary lesion may require resection, whereas transbronchoscopic removal of the endobronchial tumor may result in cure. Because of these differences, the polypoid tumors are separated from the general group of hamartomas of the lung. Twelve cases of endobronchial polypoid hamartochondroma have been collected from the literature and are reported with one additional patient treated at Duke Hospital. The pertinent facts concerning these thirteen patients were abstracted and summarized in Table I.

There are in the literature ninety-eight cases of hamartoma of the lung excluding the thirteen cases of the polypoid type. In 1936 Hickey and Sampson<sup>1</sup> collected thirty-six cases and reported two of their own. Verga<sup>2</sup> added twenty more cases in 1939 including three of his own. Twenty-three personal cases in addition to thirteen cases from the literature were reported by McDonald, Harrington, and Clagett<sup>3</sup> in 1945. Since that time Poney, Selfert, and Simon and Ballou have reported three cases. Schafer and Scott<sup>4</sup> recently reported an intrapulmonary hamartoma composed mainly of cartilage, removed by lobectomy. A solitary metastatic lesion from a bone tumor of the arm was suspected, but a benign lesion could not be excluded.

**Pathology**—In 1904 Albrecht<sup>5</sup> stated hamartomas are tumor-like malformations in which occur only an abnormal mixture of the normal components of the organ. The abnormality may take the form of a change in quantity

arrangement or degree of differentiation or may comprise all three. The deduction to be drawn from histologic examination of these formations is that they have originated in an abnormal mixing of the normal elements or from disturbance of their development. The exact origin of endobronchial polypoid hamartochondromas is in doubt. Ficken,<sup>1</sup> Blecher<sup>11</sup> and Spleen<sup>12</sup> believed these tumors to be outgrowths of the bronchial rings. Slegert,<sup>13</sup> Spuler,<sup>14</sup> Paul,<sup>15</sup> and Moore<sup>16</sup> reported elastic fibers in the cartilaginous tissue of the tumors in their respective cases. Since elastic fibers are not present in normal bronchial cartilage this was cited as evidence favoring an embryonal anlage as the site of origin.

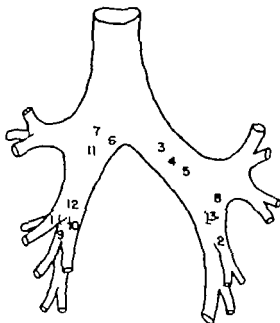


Fig. 1—Showing location of thirteen reported hamartochondromas.

The location of the thirteen tumors is indicated in Fig. 1. Grossly the tumors appear bright pink in color, spherical in shape with a nodular surface. The stalk may be more narrow than the tumor mass. The chondromas are firm and cut with resistance. Microscopically abundant cartilaginous tissue is seen frequently divided into plaques or islands by fatty tissue, cavernous blood spaces, and connective tissue. Ossification in some areas of the cartilage may occasionally be seen. The tumors are well encapsulated, and the bronchial surface covered by epithelium usually cylindrical in type. There is no peribronchial reaction in any.

**Clinical Material.**—In the series analyzed the average age of the patient was 34 years, the youngest was 21 and the remainder were over 40 years of age. Of the thirteen cases, eight were men, four women and the sex of one was not recorded.

TABLE I

UTERO	AGE (Yr.)	SEX	Symptoms	Exam	X Ray	Prognosis- Copy	Treatment	Autopsy
L. Bergeria	61	F	(Autopsy finding)					33 by 23 mm in right middle lobe bronchus; cartilage surrounded by connective tissue epithelial structures, and carcinomatous blood sinuses; becomes behind obstruction
Chuan	65	F	(Autopsy finding)					20 by 20 mm in left lower lobe bronchus, islands of calcification in hyaline cartilage, fat all scattered glands; bronchiectasis
3 Apple	1	F	(Autopsy finding)					40 mm. in left main bronchus; cartilage with basophilic fibers, with dilated vascular lumen, and connective tissue
4 E. L. L.	41	F	Cough 10 years left, blood streaked sputum for 2 1/2 yr.	Bronchiectasis with consolidation of left lower lobe		Visualized	Extensive broncho- scopy recovery	13 by 60 mm. left main bronchus; cartilage embedded in fatty tissue, covered by epithelium
5 E. L. L.	51	M	Chest pain and cough 10 years left sputum and fever for 3 mos.	Bronchiectasis on left	Opaque over left side		Open drainage of pyemia dead	10 mm. in left main bronchus covered epithelium (tissue); bronchiectasis and consolidation, left
6. S. L.	47	F	Bronchiectasis in dyspnea and orthopnea for 4 yr	Consolidation on right	Areas of consolidation on right	Visualized	Extensive broncho- scopy recovery	40 by 10 mm in right main bronchus cartilage sur- rounded by connective tissue
7. C. L.	53	M	Markedly prolon- gated cough for several months				Dead	25 by 16 mm in right main bronchus cartilage; lumen narrowed

Case	Sex	Age	At time of death	Place of death	Interval between onset and death	Time of death	Time of death	Time of death
9	Male	69	M	At home	10 years	10 years	10 years	10 years
10	Female	64	M	At home	10 years	10 years	10 years	10 years
11	Female	60	M	At home	10 years	10 years	10 years	10 years
12	Female	57	M	At home	10 years	10 years	10 years	10 years



The duration of symptoms varied from three months to twenty-five years. The symptoms were grouped as those due to the tumor itself and those which were the result of bronchial obstruction, either partial or complete. The symptoms due to the tumor itself were cough, frequently severe wheezing, chest pain and discomfort, dyspnea, sputum, hemoptysis or streaking, and frequent chest colds. When the tumor occluded a large bronchus the distal bronchi were dilated and the lung behind the obstruction became atelectatic and infected. Pneumonitis, bronchiectasis, or lung abscess followed. The symptoms resulting from these changes were increased cough, production of purulent sputum, pleuritic pain and dyspnea. The usual symptoms of toxicity as weakness, chills, spiking fever and increased fatigability then developed. The final symptoms were those associated with an overwhelming pulmonary infection.

The local signs of the tumor partially occluding a bronchus were few. A wheeze which could be localized was occasionally present and aided in differentiation from bronchial asthma. Signs of recurrent attacks of pneumonia were found. The signs associated with occlusion of a large bronchus were those of atelectasis, bronchiectasis, lung abscess, or empyema.



Fig. 2.—Roentgenograms of patient J. J. showing increased density due to abscess in upper segment of left lower lobe.

**Diagnosis.**—In the diagnosis of endobronchial polypoid hamartocarcinoma of the bronchus, x-ray examination was of value in revealing the changes associated with occlusion of a bronchus. Bronchial lipiodol studies showed failure of a lobe (Cases 7 and 10) or a segment (Case 13) to fill with the radio-paque material. In one patient (Case 11) the terminal cone-like configuration of the intrabronchial lipiodol suggested a bronchial polyp. The tumor was visualized in six instances at bronchoscopy (Cases 4, 6, 10, 11, 12, and 13).

**Treatment**—Bronchoscopic removal was successful in five patients (Cases 4, 6, 10, 11 and 12). Lobectomy was performed in one (Case 13) because of inaccessibility of the tumor by bronchoscopy. The results in both types of treatment have been excellent. The remaining cases either progressed to a fatal issue or the tumor was an incidental finding at autopsy.

# CASE REPORT

J. J., 37, white male, admitted on May 30, 1947 because of productive cough and loss of three ears duration. In 1944 he had febrile illness diagnosed as influenza. From that time recurrent episodes of fever with increased cough and weakness had occurred. For several months he had coughed up daily one-half cupful of odorless purulent sputum (rust blood). The physical examination was essentially normal. There was no cyanosis or leukocytosis. Sputum showed many polymorphonuclear leucocytes and many coccipar bacteria and streptococci, which on culture were both hemolytic and nonhemolytic. The x-ray films are shown in Figure 1.

Bronchoscopy showed a smooth, slightly lobular pinkish, polypoid lesion arising from the posterior wall of the left lower lobe bronchus. Several attempts to biopsy the lesion were futile because of its location. Thoracotomy was performed under endotracheal ethylene anesthesia. The superior and medial segment of the left lower lobe were resected. Left lower lobectomy was carried out. The postoperative course was essentially uneventful.

**Pathology**—(Growth 10 by 10 mm, hard, pedunculated tumor arose from the most proximal part of the bronchus in the superior segment of the left lower lobe producing obstruction of the bronchus and necrosis distally. The tumor was well encapsulated. Microscopic study showed typical chondroma.

# SUMMARY

Endobronchial polypoid hamartochondroma is a rare lesion, only thirteen cases having been reported. These tumors are clearly related to, but should be differentiated from other hamartomas of the lung. The endobronchial polypoid hamartochondroma produces symptoms by partial or complete bronchial obstruction. If accessible by bronchoscopy removal is indicated. If inaccessible at bronchoscopy or if permanent pulmonary damage has followed the obstruction, lobectomy may be indicated.

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### PRIMARY SARCOMA OF THE GREATER OMENTUM

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PRIMARY tumors of the greater omentum are infrequent and primary sarcomas are much more so. Up until 1934 only seventy five cases of primary sarcomas of the greater omentum were recorded these were reviewed by Hanson and Samson. Since that time other cases have been added by Sannes and Kerum in 1934, Menne and Lilje in 1936, Levy and Pund in 1940 and Lawler, Fox, and Cohen in 1946. In view of the rarity of this neoplasm and the peculiar diagnostic difficulties associated with it, the reporting of another instance of the disease is appropriate.

## CASE REPORT

F K aged 51 years, was admitted to the Wisconsin General Hospital Aug 9 1940, with the chief complaint of pain in the loins. He stated that he had had swollen loins for three or four years without symptoms. Eight months prior to admission, after eating heavy meal, he developed right sided loins pain which was of short duration and disappeared spontaneously. A week before admission he again developed loins pain which was persistent and exacerbated by eating. During this period he noticed that the abdomen increased in size and became tense. He also noted that the right side of his chest expanded less completely than the left side. He also noted that the right side of his chest expanded less completely than the left side. He also noted that the right side of his chest expanded less completely than the left side.

By peritoneoscopy no B. 1 was found in the abdomen, but in the right upper quadrant there are many fibrous adhesions about lesion considered to be not vital although no primary B. 1 was detectable. Complete ray studies of the abdomen radiated soft tissue mass in the upper midabdomen and showed stomach high & high but which emptied in normal rapidly. The small bowel was packed to the left and the colon as unobstructed through the left side as displaced laterally. In the ray view of the chest the diaphragm was normally low but in some compression telereads in the bases of both lungs.

The laboratory findings listed normal urinal = hemoglobin 0.7 Gm. per cent red blood cell 3.9 m. Hb and h+ blood cell 14,100 is the following differential 82 per cent neutrophils 3 per cent lymphocytes and 6 per cent monocytes blood sugar 100 mgm per cent and serum urea nitrogen 10 mgm per cent are his normal limits. Prothrombin was 100 per cent and his per cent age serum protein was 6.4 Gm per 100 with an albumin/globulin ratio of 1.1

A laparotomy performed Sept 3, 1940 disclosed 1 spe suggesting worm burr observed the area. There considerable bleeding on dissection, so that he exact limit of the tumor could not be well determined. A biopsy is taken, however and subsequent report from same. The markedly postoperative response was satisfactory. Subsequently the patient condition deteriorated gradually and death occurred one month later on Oct 1, 1940.

The right pleural surface was back up to and the considerably enlarged and I thought it was an old bull's head was formed. There was a small amount of fluid in the right pleural space. The right pleural surface was back up to and the considerably enlarged and I thought it was an old bull's head was formed. There was a small amount of fluid in the right pleural space.

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**Microscopic Examination.**—Microscopically the neoplasm as exposed preoperatively of large, spindle-shaped cells, compactly arranged in linear and nested groups (Fig 1) and intimately associated with numerous small capillary vessels, many of which contained erythrocytes. The cell borders are vague, and the cytoplasm is eosinophilic opaque, and many contained clear structureless coales (Fig 2). Mitotic figures are common. In areas, vacuoles of several cells predominated and appeared as coales. Erythrocytes were not conspicuous. The nuclei were large spindle-shaped, hyperchromatic and occasionally are indented and flattened by the vacuoles. This histologic pattern is replaced occasionally by myxomatous type of tissue, in which the spindle cells are few and hyperchromatic, and appeared to float in the homogeneous eosinophilic matrix (Fig 3). The various metastases revealed

On the edge adjacent to the liver tissue the cells were vacuolated and similar to those seen in the anastomosis, although here the nodular arrangement is more evident.

Fig 1

Fig 2

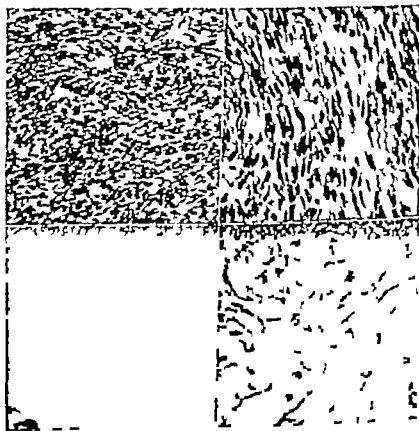


Fig 3

Fig 4

Fig 1—Section from osseous neoplasm in which the spindle-shaped cells are closely related to capillary vessels (a. = anastomosis and vessels.)

Fig 2—relation to capillary vessels  
epithelial cells  
of the osseous tissue and vessels.

## DISCUSSION AND CONCLUSION

This tumor falls grossly into the category of the diffuse type as indicated by Levy and Pund. It satisfies the criteria proposed by McDonald<sup>4</sup> for authentication of omental sarcoma in that its extent in the omentum indicates this structure as the origin and that histologically it is a sarcoma, which has metastasized. The interpretation of the significance of the vascular pattern requires circumspection. It would be simpler certainly to follow McDonald's example and classify this as sarcoma merely until the vexed question of the endotheliomas is settled. There are however several facts which deserve fuller consideration. Most significant are the formation of intracytoplasmic vacuoles and the fusion of such vacuoles from several cells to form a distinct cell lined space. This pattern of cell behavior resembles that described by Kettle and Row in their cases of vascular endotheliomas. Of considerable importance in the interpretation of the tumor is the leaf-cut vascular structure of the hepatic metastasis, which in some parts resembles a cavernous angioma. Whether this is regarded as a source or an extension of the neoplasm, its vascular nature confirms the origin of the tumor as endotheliomatous in this instance. It is pertinent to indicate that in none of its parts does the lesion resemble a liposarcoma, either histologically or cytologically (Stout)<sup>5</sup> and it is unlikely that fat stains are of use in excluding liposarcoma any more conclusively than cytologic criteria because whereas liposarcomas may be poor in fat degenerative sarcomas may contain much fat material. It is, moreover possible that infiltrative neoplasm incorporate adipose tissue a contingency most likely to be encountered in predominantly a lipose tissues such as the omentum. The tumor under consideration complies with the criteria of a primary omental sarcoma and conforms in its structure to the endotheliomas described by Kettle and Row. It closely resembles those designated as endotheliomas by Levy and Pund. While liposarcoma cannot be rigidly excluded, it is unlikely because of the absence of certain cytologic features.

## SUMMARY

A case of primary sarcoma of the omentum is described. It is classified as an angioendothelioma, because of its peculiar structure and the obviously vascular nature of the metastases.

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**Microscopic Examination.**—Microscopically the neoplasm was composed predominantly of large spindle-shaped cells, compactly arranged in linear and nested groups (Fig 1) and intimately associated with numerous small capillary vessels, many of which contained erythrocytes. The cell borders were vague, and the cytoplasm eosinophilic, opaque and granular, containing few structureless nucleoli (Fig 2). Mitotic figures were common. In areas, nucleoli of several cells protruded and appeared to coalesce. Reticulum was not conspicuous. The nuclei were large, spindle-shaped, hyperchromatic, and occasionally were indented and flattened by the nucleoli. This histologic pattern was replaced or replaced by a nodular type of tissue, in which the spindle cells were few, small, protruded, and appeared to float in the homogeneous eosinophilic matrix (Fig 3). The various nest states resembled the parent neoplasm closely except the one in the liver which had a very vascular structure (Fig 4). In its center the vessels were large and irregular, and filled with erythrocytes. Peripherally the vessels were smaller with walls composed of two or three cells, and empty lumens. On the edge adjacent to the liver tissue, the cells were associated and similar to those seen in the omentum, although here the vascular arrangement was more or less

Fig 1

Fig 2

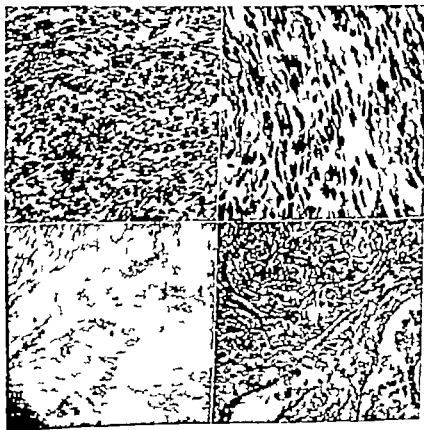


Fig 3

Fig 4

Fig 1.—Section from omental neoplasm, in which spindle-shaped cells are common.

patient in a body cast for six or eight weeks. The main point of treatment however is that the patient should not bear weight on the involved extremity for at least six months from the time of the accident. While this is a very difficult rule to enforce patients can be convinced that unless this course is followed they are likely to have serious permanent disability. The progress of healing of the bone can be followed by frequent roentgenograms to observe the density or contour of the head of the femur. Even after a period of six months protection and after the patient is allowed to begin weight-bearing he should have roentgenograms taken every two or three months for one year to make certain that no late destructive changes are developing in the head of the femur. If degenerative changes begin to appear it is necessary for the patient to resume the use of crutches.

The recognition of the great importance of circulatory changes following traumatic dislocations of the hip has completely revolutionized the plan of treatment. It has focused attention on the total inadequacy of former treatment and the possibility of reducing the residual permanent disability that follows this serious injury.

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## Editorial

### Traumatic Dislocation of the Hip

WHILE it is not a common accident, traumatic dislocation of the hip is a potent source of permanent disability. The circulatory damage which produces the incapacity can occur after partial dislocation, fracture-dislocation, central dislocation, or the more frequent posterior and dorsal dislocations. From 30 to 60 per cent of those who receive this injury suffer late symptoms in the hip such as pain, stiffness, and pronounced limp. The old statistics on the frequency of such dislocations are of no value now because of the constantly increasing number of automobile accidents which produce them.

Since the time of Hippocrates, surgical textbooks have described the anatomic types of displacement, the methods of diagnosis, and the various manipulations needed to reduce dislocations. Unfortunately there was no mention of the more important aftercare or the need for protection of the joint during the late stages of healing. As a consequence this injury was almost always followed by preventable destructive changes in the joint. Only in the last ten or twenty years has sufficient knowledge been gained about the circulation to the hip to indicate proper aftercare of these cases. Studies on the circulation of the hip after fractures of the neck of the femur have revealed the precarious blood supply of the head of the femur and its marked vulnerability to injury. This knowledge has demonstrated the need for long protection of hips that have been dislocated. Moreover it has been observed that those patients who have received other injuries that required long bed rest have ultimately gained better hip function than the patients who bore weight early.

Röntgenograms of a dislocated hip of course do not reveal the extensive soft tissue damage or the amount of displacement of the head of the femur at the moment of the accident. Modern anesthetics, supplemented with curare and other relaxing drugs, make it possible to reduce hip dislocations without undue force. In fact gentle manipulation is adequate in most cases, and they decrease the danger of further damage to the soft tissues. The usefulness of this is that there is seldom any need for open reductions of dislocations of the hip. Even when there are fractures through the head of the femur it is generally possible to replace the hip without open operation. The initial maceration of the tissues about the hip, the tense hematomata and the subsequent open reduction are frequently followed by pathologic calcifications about the joint, with ultimate stiffness.

After reduction of dislocations of the hip the patient should be kept in bed for two or three weeks or until the soft tissues have recovered from the effects of the accident. Then crutches or a weight-bearing brace should be used for many months. If there has been an accompanying fracture of the acetabulum, it may be necessary to maintain traction on the leg or to place the

The ultimate pursuit of our discussion will, therefore include anatomic considerations, etiologic factors, and treatment thereof, since our primary premise was the diminution or absence of painful and thermal stimuli to the involved areas. The presence of hypesthesia or varying degrees of anesthesia, whatever was the prevailing situation, made for the numerous injuries (especially burns) sustained by these patients to the already affected member.

In our anatomic considerations, we are primarily concerned with the two components of the sciatic nerve namely the posterior tibial and common peroneal nerves and the three main peripheral nerves of the upper extremity that is, the median, ulnar and radial component of the brachial plexus. According to this anatomic division, many patients will then be seen to have sustained multiple injuries, some to a single extremity others to any combination of the four.

#### LOWER EXTREMITY

In so far as the lower extremity was concerned, paralysis of the posterior tibial nerve (Fig. 1-1) rendered itself most problematic, especially regarding the prophylaxis of ulcer formation. This we found of markedly more significance than any and all treatment which we could offer once a disease process had been established. A good common sense regime of preventative treatment appeared, then, to be the *sine qua non* and all measures instituted were directed along these channels. Personal neglect and ignorance of the seriousness of the situation on the part of some of the patients were also obstacles which we had to overcome.

As one can readily see the sensory distribution of the posterior tibial component of the sciatic nerve is in an area which bears the entire weight of the body and is most vulnerable to trauma, extreme thermal states, and pressure either from ill fitted shoes or full weight bearing over bony prominences. In several cases we had also to contend with residuals from trench foot with some patients who had active infection of epidermophytosis, and with still others who had a disturbed circulation secondary to severe diabetes.

Our greatest problem was the development of calluses over bony prominences, especially over the heel of the metatarsals. If these calluses were not closely observed and early treatment instituted they usually followed a progressive course with ultimate undermining and subsequent ulceration and secondary infection. Prophylactic treatment then being of primary concern the following regime was outlined and to this we rigidly adhered.

Mental alertness was first and foremost in our teachings to the patient. He was constantly reminded of the fact that he had to watch closely and protect the involved extremity for there were no longer the so-called messengers in his foot to warn him of the onset of an deleterious or menacing stimuli.

Foot hygiene was another must in the agenda. The feet were to be bathed twice daily followed by a thorough dusting with talcum or regulation foot powder. White socks were preferred and were to be changed daily.

When partial or full weight bearing was subsequently allowed the problem of shoes was very much intensified and required special construction for

# Recent Advances in Surgery

EDITED BY ALFRED BLALOCK, M.D.

## AN ANALYSIS OF THE TREATMENT OF TROPHIC ULCERS

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SINCE the time of Hunter treatment of trophic ulcers has always been a matter of speculation, and, as one reviews the literature, realization of this fact is borne out for there is a manifold amount of prescribed, as well as the so-called specific, treatment for similar as well as identical ulcerative lesions. However it is not within the scope of this paper to catalogue the entire gamut of trophic ulcers, but only to bring to the fore one type with which the general practitioner as well as the surgeon, will have to contend, as an aftermath of World War II. These are the trophic ulcers which arise secondary to peripheral nerve injuries. In our series, the majority of the latter represented a complete anatomic severance of the nerve with but few instances of physiologic dehiscence only.

Our purpose, then, is to summarize routine of treatment which we have found to be most efficacious, after having observed and treated some 650 patients, who exhibited a total of 723 nerve lesions.

The types of patient treated were essentially all battle casualties, with nerve injuries to the extremities. The age group varied between 18 and 30 years, and each had been in continual hospitalization for some two to three years following injury.

It is agreed that the presence of certain skin changes in these patients associated with long-standing nerve injuries, and in themselves loosely designated as trophic in nature are very definitely and unequivocally the result of disuse of the extremity rather than of definite vascular damage and impairment. This was further borne out by analysis of these cases, which demonstrated that, although most of them were accompanied by or occurred concomitant with, fractures, an associated vascular injury was the exception rather than the rule. Certainly less than 1 per cent of the patients required a major vessel ligation at the time of injury. This, then, allows us to suppose that these were all true trophic ulcers, in accordance with the strict definition of the term. In addition wherever sympathectomy was carried out, it was so done because of an associated reflex sympathetic dystrophy rather than being executed specifically for purposes of increasing the peripheral circulation.

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each patient. Fundamentally there were a few basic forms from which we worked, and from these developed a shoe which we felt satisfactory to conform to the special needs of the patient. These precautions were necessary in order to obviate any tightness, with consequent pressure by the shoe for most of the patients developed a dependent edema after several hours of weight-bearing.

Fig. 1, I to E serves to exemplify these particular walking aids. Because of the primary nerve paralysis, each shoe had also a brace attached. The further addition of a T strap (Fig. 2, F) was necessary in those cases where there was varus or valgus deformity of the ankle.

The patient then either was prescribed an orthopedic convalescent shoe (Fig. 3, A) or else had the top of the low-quartered shoe split to the toe and a lacer adjustment applied (Fig. 3, B). When ulcerations developed over the insertion of the tendo achillis, the counter of the shoe was removed and a lacer adjustment applied (Fig. 3, C). Occasionally when marked contraction of a single digit occurred, as usually happened to the great toe we had but to excise a section from the dorsum of a normal shoe to prevent pressure in this region (Fig. 3, D).

In cases with plantar callouses or healed ulcerated areas, sponge rubber or felt insoles were inserted cut out and tapered to conform with the callus or bony prominence on the plantar aspect of the foot (Fig. 4, A and E). It was further noted that shoes had to fit snugly but not tightly in order to obviate friction burns which usually resulted from a loosely fitted shoe.

Patients were divided into four categories, according to the type of active therapy required, as follows:

Category I Cases with hyperkeratotic callouses but with no evidence of infection

Category II Ulcerative lesion with secondary infection

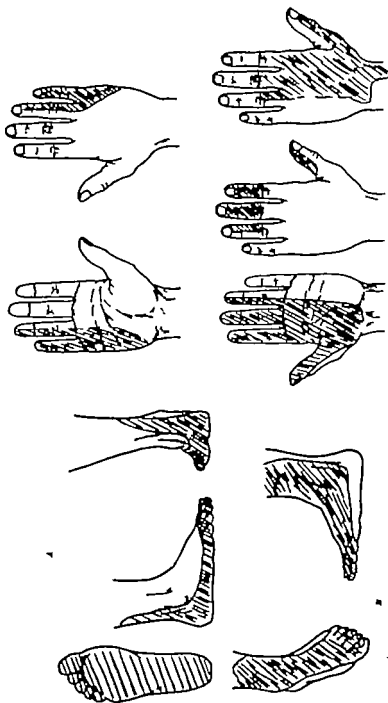
Category III Ulcerative lesion with secondary cellulitis and/or lymphangitis

Category IV Ulcerative lesions secondary to burns

Before considering each individually however the following routine requirements were insisted upon in all categories:

- 1 In any case weight-bearing on the involved extremity was not permitted.
- 2 During the course of dressings, a liberal tape was never to be applied directly to the skin on the involved extremity. Such a procedure in the presence of certain trophic changes might add an additional insulting stimulus.
- 3 No shoe was to be worn on the involved extremity.
- 4 (a) Elevation of the extremity to a level of 20 to 30 degrees above the horizontal was to be carried out for at least six to eight hours during each waking day.
- (b) Ambulatory patients were never permitted to place the extremity in a dependent position over prolonged period of time. When sitting, the foot and leg were to be elevated on a second chair or stool, to at least the horizontal position.
- 5 Fifteen to thirty minutes of active exercising of the involved extremity.

and by padding privately secured furnished and leather or felt shoes, which they are less up and about, to protect against the minimal amount of everyday trauma.



A Sensory loss resulting from posterior tibial nerve palsy. B Sensory loss resulting from common peroneal nerve palsy. C Sensory loss resulting from median nerve palsy. D Sensory loss resulting from ulnar nerve palsy. E Sensory loss resulting from radial nerve palsy. F Sensory loss resulting from posterior tibial nerve palsy. G Sensory loss resulting from posterior tibial nerve palsy. H Sensory loss resulting from common peroneal nerve palsy. I Sensory loss resulting from median nerve palsy. J Sensory loss resulting from ulnar nerve palsy.

each patient. Fundamentally there were a few basic forms from which we varied, and from these developed a shoe which we felt satisfactory to conform to the special needs of the patient. These precautions were necessary in order to obviate any tightness, with consequent pressure by the shoe for most of the patients developed a dependent edema after several hours of weight-bearing.

Figs. 2, A to E serves to exemplify these particular walk-in shoes. Because of the primary nerve paralysis, each shoe had also a brace attached. The further addition of a T trap (Fig. 2, F) was necessary in those cases where there was varus or valgus deformity of the ankle.

The patient then either was prescribed an orthopedic convalescent shoe (Fig. 2, A) or else had the top of the low-quartered shoe split to the toe and a lacer adjustment applied (Fig. 2, B). When ulcerations developed over the insertion of the tendo achillis, the counter of the shoe was removed and a lacer adjustment applied (Fig. 2, C). Occasionally when marked contraction of a toe digit occurred, as usually happened to the great toe, we had but to excise a section from the dorsum of a normal shoe to prevent pressure in this region (Fig. 2, D).

In cases with plantar calluses or healed ulcerated areas, sponge rubber or felt insoles were inserted, cut out and tapered to conform with the callus or bony prominence on the plantar aspect of the foot (Fig. 2, A and E). It was further noted that shoes had to fit snugly but not tightly in order to obviate friction burns which usually resulted from a loosely fitted shoe.

Patients were divided into four categories, according to the type of active therapy required, as follows:

Category I Cases with hyperkeratotic callouses but with no evidence of infection.

Category II Ulcerated lesions with secondary infection.

Category III Ulcerated lesions with secondary cellulitis and or lymphangitis.

Category IV Ulcerated lesions secondary to burns.

Before considering each individually, however, the following routine requirements were insisted upon in all categories:

1. In any case weight-bearing on the involved extremity was not permitted.
2. During the course of dressings, adhesive tape was never to be applied directly to the skin on the involved extremity. Such a procedure in the presence of certain trophic changes, might add an additional insulting stimulus.
3. No shoe was to be worn on the involved extremity.
4. (a) Elevation of the extremity to a level of 30 to 35 degrees above the horizontal was to be carried out for at least six to eight hours during each waking day.
- (b) Ambulatory patients were never permitted to place the extremity in a dependent position over prolonged periods of time. When sitting, the foot always were to be elevated on a second chair or stool, to at least the horizontal position.
5. Fifteen to thirty minutes of active exercising of the involved extremity

\*All our patients received personal, constant care, whether or not they were able to stand and about to protect against the minimal amount of erysipelas infection.

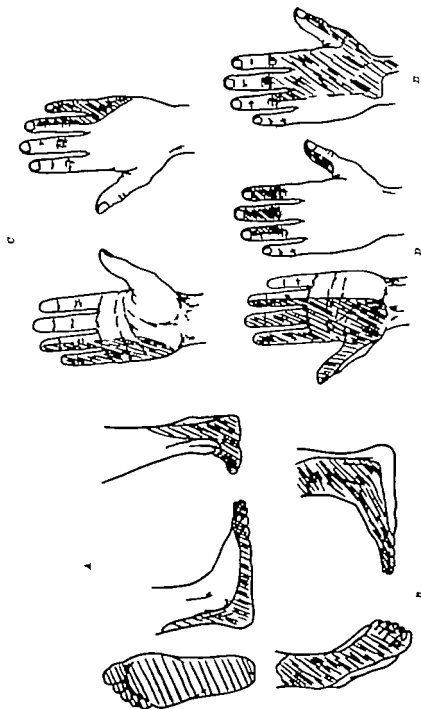


Fig. 1.—A, sensory loss resulting from posterior tibial nerve paralysis; B, sensory loss resulting from posterior peroneal nerve paralysis; C, sensory loss resulting from ulnar nerve paralysis; D, sensory loss resulting from median nerve paralysis; E, sensory loss resulting from radial nerve paralysis; F, sensory loss resulting from radial nerve paralysis.

each patient. Fundamentally there were a few basic forms from which we worked, and from these developed a shoe which we felt satisfactory to conform to the special needs of the patient. These precautions were necessary in order to obviate any tightness, with consequent pressure by the shoe, for most of the patients developed a dependent edema after several hours of weight-bearing.

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In cases with plantar callosities or healed ulcerated areas, sponge rubber or felt insoles were inserted, cut out and tapered to conform with the callus or bony prominence on the plantar aspect of the foot (Fig. 1, I and E). It was further noted that shoes had to fit snugly but not tightly in order to obviate friction burns which usually resulted from a loosely fitted shoe.

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Category I Cases with hyperkeratotic callosities but with no evidence of infection.

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Category III Ulcerative lesion with secondary cellulitis and/or lymphangitis.

Category IV Ulcerative lesions secondary to burns.

Before considering each and individually, however, the following routine requirements were insisted upon in all categories:

1. In any case weight-bearing on the involved extremity was not permitted.

During the course of dressings, adhesive tape was never to be applied directly to the skin on the involved extremity. Such a procedure in the presence of certain trophic changes, might add an additional irritating stimulus.

2. No shoe was to be worn on the involved extremity.

3. (a) Elevation of the extremity at a level of 20 to 30 degrees above the horizontal was to be carried out for at least six to eight hours during each waking day.

(b) Ambulatory patients were never permitted to place the extremity in a dependent position over prolonged periods of time. When sitting the foot and leg were to be elevated on a second chair or stool, to at least the horizontal position.

4. Fifteen to thirty minutes of active exercising of the involved extremity

if any patient previously occurred, for hard soft leather or felt shoes, which they are worn up and about, to protect against the mechanical aspects of everyday trauma.



four times a day was mandatory. This was carried out, as much as possible, under the direction and guidance of the physiotherapy department.

Those patients considered under Category I, as outlined, were then treated according to the following regime

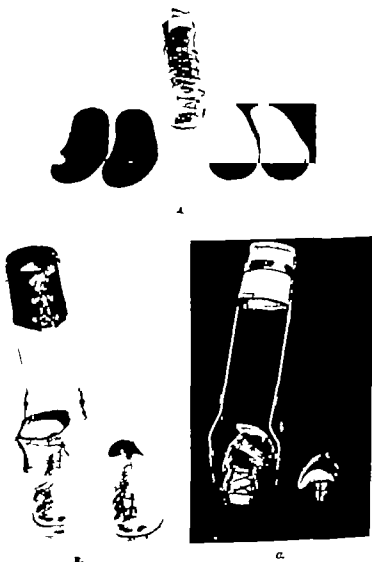
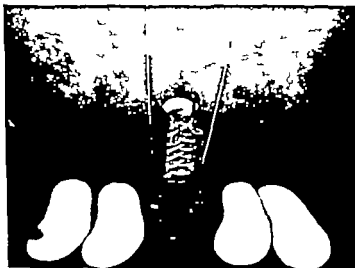


Fig. 1. A B and C—A, Orthopedic corsetment shoe (exterior, top) and corset belt. B, Low-quartered shoe, split to see heel adjustment applied. C Low-quartered shoe, corset removed and heel adjustment applied.

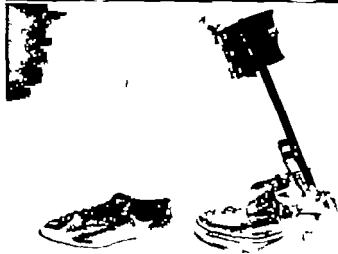
Warm (50 per cent) borax and soaks were applied to the involved area, three times a day. A petrolatum gauze dressing was applied to the calloused area, after each soaking. When the callus had become well demarcated, it was trimmed to its base. In order to return tone to the soft tissues, the foot was then given alcohol massages three times a day for one week.

Following this, the patient was fitted with a suitable shoe such as has already been described, and was then ready to begin gradual weight-bearing.

E



D



F

Fig. 2. D, E and F.—D Low-quartered shoe. E dorsally extending wedge sole. F Orthopedic shoe elevator shoe. (posterior view) not visible. F T-stra on lateral aspect of low-quartered shoe for arched deformity. Braces and lower adjustment not usually applied.

This was, at first, limited to thirty minutes daily but later increased by degrees until full weight-bearing on the involved extremity was finally tolerated.

Lesions assigned to Category II required the selection of those therapeutic agents which demonstrated an antiseptic, as well as a keratogenic, effect. Those considered most efficacious were iodoform gauze, scarlet red ointment, and chloroform, and were employed in this order. Accordingly we found that in but a very few instances did we have to change our therapeutic agent. This exhibited itself mainly when the patients manifested a definite allergy to the drug used, or in those instances where they were resistant to it.

The exact mode of treatment consisted of the following. The weeping wound was soaked in (5 per cent) boric acid solution for two hours daily after which one of the afore-mentioned therapeutic agents was applied locally. This procedure was then continued until the ulcer bed showed evidence of healthy granulation tissue, with progressive epithelization, and a relative drying of the wound. When this had manifested itself soaking was discontinued and only the particular therapeutic agent applied. In most instances, this was iodoform gauze. The latter was then continued until the ulcer had become fully epithelialized. Final treatment consisted of proper shoe fitting and progressive weight bearing as previously outlined.

It is best to interject at this time that in several cases, there was noted a severe local reaction, ascribed to the use of iodoform gauze. This manifested itself by swelling, redness, vesiculation, and pruritus. These manifestations were however well controlled by the use of Burow's solution (1:1000) soaks and the oral administration of calcium gluconate tablets.

Category III, namely those ulcers complicated by a cellulitis and/or diffuse lymphangitis of the entire extremity presented a somewhat more comprehensive problem.

The patient was kept at absolute bed rest with temperature, pulse and respiration recordings every four hours. A white blood count and sedimentation rate were taken twice weekly. The involved extremity was elevated on its side to three pillows, and was kept in continuous hot packs for approximately forty-eight hours. Application of a penicillin pack (500 units per cubic centimeter) directly to the ulcer site preceded the usual boric acid solution wet dressing. This period of time was found usually sufficient to abort the acute phase of the infection, without unduly macerating the adjacent soft tissues. Since this usually involved the treatment of many almost completely anesthetic areas, it was absolutely imperative that the temperature of the solutions used be rigidly regulated so as to obviate the additional insult of superimposed burns.

In addition to the local application penicillin was also administered subcutaneously usually in doses of 100,000 units every three hours, and for such period of time as was necessary to reduce the white blood count and sedimentation rate to normal level. At this time there was, most usually, a complete remission of the cellulitis and/or lymphangitis present.

After cessation of the acute phase the patient was continued on the regimen exactly as outlined under Category II.

Ulcerative lesions occurring secondary to burns, namely those considered in Category IV focused our attention primarily on the resultant ulcer. Since the involved area rarely exceeded 5 cm. in diameter shock per se was never of therapeutic consequence.

Our course of treatment for these lesions was one of débridement with the subsequent application of a softening agent, usually petrolatum gauze. Dressings were changed on the average of two to three times a week, since more frequent disturbance of the wound would tend to retard rather than stimulate healing. Scarlet red ointment applied to those ulcerative areas where delayed healing was a factor appeared to enhance the healing processes.

#### COMMON PERONEAL COMPONENT

In so far as the common peroneal component of the sciatic nerve was concerned those ulcers which occurred were usually in its autonomous domain (Fig 1, B). These resulted primarily through neglect and came about as an aftermath of overzealous or faulty treatment usually at the hands of the patient himself. Many times, he might thoughtlessly employ the use of a hot water bottle, or place the injured extremity against a hot radiator or heater being grossly unaware of the resulting burn to the anesthetic area. Callosities, arising secondary to pressure from ill-fitted shoes, were also a cause of subsequent ulceration in this group.

The treatment employed for both burns and secondary ulcerations was exactly as that already described.

#### UPPER EXTREMITY

In considering the upper extremity we found that burns were of primary concern, and that lacerations and other traumatic lesions were secondary. Any or all of these were usually brought about following an attempt to use the injured extremity for one or another reason. Cigarette burns were perhaps most common. Where there was ulnar nerve involvement (Fig 1 C) the patients incurred the burns by having rested the anesthetic hand on a hot object.

Perhaps the largest group of cases herein concerned were those with median nerve injury (Fig 1 D). As previously stated, it was the burning cigarette which was most often the offending agent with involvement of the index and long fingers. Radial nerve injuries per se seldom rendered themselves problematic and were of small concern in our series (Fig 1 F).

Those ulcerations of the upper extremity which were resultant from burns, as well as any other superimposed complications were treated exactly as outlined previously for similar conditions of the feet.

#### DISCUSSION

The average length of treatment for those in Category I was approximately four weeks; those in Category II ten weeks; those in Category III twelve weeks; and those in Category IV fourteen to eighteen weeks.

In Table I we have represented a complete analysis of all the patients treated over a period of one year from Sept 1 1946 to Aug 31 1947. During

these twelve months, amputation was carried out in but five instances, and in one of these only because of a severe tendo achillis shortening and marked deformity about the ankle which could not be corrected by surgery in the presence of the nerve paralysis. All patients discharged showed a complete healing of the ulcers, and each had been given a trial period of full weight-bearing for at least forty five to sixty days in advance of leaving the hospital.



FIG. 3.—H. B. Complete paralysis of posterior tibial nerve (irreversible, marked atrophy and deep draining ulcer over heel; discharged on full weight bearing.

Figs. 3, 4, and 5 are representative of the type of lesion with which we were concerned. One of these (J. C.) required a below knee amputation in spite of complete healing of a huge ulcer. This was necessitated because of the marked tendo achillis shortening and equinovarus deformity of the involved foot, together with an excessive degree of ankylous about the ankle. Numerous attempts at correction of this deformity by conservative measures, that is, wedging in casts and splinting were all unsuccessful, and, of course, surgical intervention was contraindicated because of the presence of an almost complete anesthesia. This unfortunate incident would then serve to stress a very



Fig 4.—R. X. P. (Colored) Complete syphilitic nerve paralysis (repaired). A Ulcerated and infected area on dorsum of great toe and medial aspect of foot secondary to (third degree) hot tar bottle burn. B Dorsal view showing areas completely healed weight bearing begun.

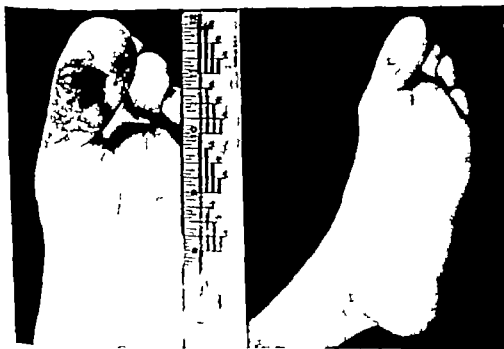


Fig 5.—J. C. Complete syphilitic nerve paralysis (repaired). A Large ulcer undermined and infected, secondary to edema in cast following attempt to correct marked equinovarus deformity and ankylosis. B Ulcer almost completely healed below-knee reposition three months later because of unsuccessful attempts at correcting these deformities. Weight-bearing impossible.

these twelve months, amputation was carried out in but five instances, and in one of these only because of a severe tendo achillis shortening and marked deformity about the ankle, which could not be corrected by surgery in the presence of the nerve paralysis. All patients discharged showed a complete healing of the ulcers, and each had been given a trial period of full weight bearing for at least forty five to sixty days in addition to leaving the hospital.



FIG. 2.—II. Complete paralysis of posterior tibial nerve (irreversible), marked eversion and deep draining ulcer over heel; discharged on full weight bearing.

Figs. 3, 4 and 5 are representative of the type of lesion with which we were concerned. One of these (J. C.) required below-knee amputation in spite of complete healing of a huge ulcer. This was necessitated because of the marked tendo achillis shortening and equinus or deformity of the involved foot together with an excessive degree of kylosis about the ankle. Numerous attempts at correction of this deformity by various measures, that is, wedging in casts and plinting were all unsuccessful, and, of course, surgical intervention was contraindicated because of the presence of an almost complete anesthesia. This unfortunate incident would then serve to stress a very

# SURGERY

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## Original Communications

### CEREBRAL ANGIOGRAPHY IN THE DIAGNOSIS OF INTRACRANIAL HEMATOMAS

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(From Otolaryngology and Third Surgical Department)

HOSPITALS with general surgical services, as well as special neurosurgical clinics, will often have to face the diagnostic and therapeutic difficulties which arise when patients are admitted with acute head injuries. Only a few surgeons get sufficient personal experience in this field of traumatic surgery and there will always be cases that will arouse doubt as to the nature and extent of the intracranial lesion.

Skull fractures are not very significant in this connection. In the treatment of closed head injuries they are of minor importance in contrast to the importance of fractures in other parts of the human body. In a series of 329 patients with craniocerebral injuries admitted to Oslo City Hospital, Third Surgical Department during the years 1937 to 1939 skull fracture was present in 81 per cent of the cases. The mortality rate was 7.6 per cent of the total number of cases, but the mortality was 16 per cent among the patients with skull fractures. A skull fracture indicates that the patient has sustained an injury of a certain degree of violence. In our experience head injury without skull fracture will prove fatally rarely. While this fact may be of a certain prognostic significance it does not imply that the fracture per se is of any importance as the cause of death.

The site of a skull fracture may give an indication of the side of the hemorrhage but this is not undisturbed. A lateral dislocation of a callosal pineal shadow is a more reliable guide but it must be remembered that this may also be seen in unilateral cerebral edema.

The chief lesions in patients with craniocerebral injuries are those pertaining to the brain and the meninges. Most of the head injuries in patients admitted to general surgical department belong to the cerebral concussion group. The treatment in these cases is conservative. Dehydration is used here with magnesium sulfate, both as a prevention against cerebral edema and also as a treatment in patients who have already developed edema. Cerebral edema may be the dominant feature of the clinical picture in certain patients.



TABLE I

DESCRIPTION	NUMBER	PER CENT OF TOTAL
Total nerve injuries	733	
Number of cases	630	
Ulcers, upper extremity	7	0.95
Ulcers, lower extremity	70	9.5
Amputations	8	0.68
Sciatic nerve paralysis (complete)	171	23.3
Posterior tibial	47	6.4
Common peroneal	90	12.3
Brachial plexus paralysis (complete)	51	7
Radial	153	17.6
Median	158	17.0
Ulnar	121	16.6
Multiple injuries	89	12.1

More than one nerve in either extremity      classes of complete sciatic or brachial plexus paralysis

cardinal point in the treatment of these patients, from the very outset of injury. That is to say that conscientious and rigorous physiotherapy is indeed a very important procedure included in the regime of therapy. This should include both active and passive motion within the limitations of the injury sustained, and, in addition the very careful application of heat, together with massage and whirlpool baths, wherever feasible. Unquestionably these measures are of supreme importance if we are to adhere to the striking significance of a program of prophylaxis.

Examination of those extremities removed at surgery (amputation) very clearly demonstrated the pathology associated with nerve paralysis and the many secondary effects produced as a result of prolonged inuse of the involved member. In each there was seen a focal fatty replacement of the muscle fibers with condensation of the nuclei into clumps and clusters, and in many areas a total absence of the fibers themselves. There was also a marked moderate degree of inflammatory change with invasion by numerous round cells. The picture was truly one of tissue atrophy. In each there was also a obliterative endarteritis of the smaller vessels, but nowhere was there vascular necrosis or significant alteration of the larger blood vessels. Pathologically, then, our original supposition that these were all ulcers of a true trophic nature seems further to be borne out.

In the final analysis, one can well rely that associated with the healing processes of trophic ulcers secondary to peripheral nerve injuries, there must be the unrelenting courage of the patient and the unwavering patience of the doctor. For it is a matter of either saving the extremity or admitting the patient to amputation and it may be said here this would mean, in many cases, a patient with a bilateral amputation, because many whom we had been treating had a previous amputation of the member on the opposite side.

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### CEREBRAL ANGIOGRAPHY IN THE DIAGNOSIS OF INTRACRANIAL HEMATOMAS

ARISTIDAN KRISTIANSEN, M.D. MONTREAL, CANADA

(From Oslo City Hospital Third Surgical Department)

HOSPITALS with general surgical services, as well as special neurosurgical clinics, will often have to face the diagnostic and therapeutic difficulties which arise when patients are limited with acute head injuries. Only a few surgeons get sufficient personal experience in this field of traumatic surgery and there will always be cases that will arouse doubt as to the nature and extent of the intracranial lesion.

Skull fractures are not very significant in this connection. In the treatment of closed head injuries they are of minor importance in contrast to the importance of fractures in other parts of the human body. In a series of 399 patients with craniocerebral injuries admitted to Oslo City Hospital's Third Surgical Department during the years 1931 to 1939 skull fracture was present in 8 per cent of the cases. The mortality rate was 7.6 per cent of the total number of cases, but the mortality was 16 per cent among the patients with skull fractures. A skull fracture indicates that the patient has sustained an injury of a certain degree of violence. In our experience a head injury with skull fracture will prove fatal only rarely. While this fact may be of a certain prognostic significance it does not imply that the fracture per se is of an importance as the cause of death.

The site of skull fracture may give an indication of the side of the hemispheric but this is not consistent. A lateral dislocation of a so-called pinnal shadow is more reliable guide but it must be remembered that this may also be seen in unilateral cerebral edema.

The chief lesion in patients with craniocerebral injuries are those pertaining to the brain and the meninges. Most of the head injuries in patients admitted to a general surgical department belong to the cerebral concussion group. The treatment in these cases is conservative. Dehydration is used here with an osmotic salt solution both as prevention against cerebral edema and also as treatment in patients who have cerebral level edema. Cerebral edema may be the dominant feature of the clinical picture in certain patients,

perhaps particularly in children. This fact is of diagnostic and the apter significance because the course of events and the symptoms in cases of cerebral edema are very similar to the symptomatology of intracranial hematomas. The effect of dehydration in these patients is therefore of considerable diagnostic value.

Cerebral contusions and lacerations, except in special cases, do not indicate craniotomy either. The differential diagnosis of contusion, or subdural and extradural hematoma, may offer great difficulties and sometimes the clinical examination fails to provide the correct diagnosis.

Intracranial hematomas, the main subject of this paper as relative in frequent lesions in patients with head injuries admitted to a general surgical department. In the series of cases from 1937 to 1939 only 1 per cent of the patients presented extradural hematomas and 1 per cent subdural.

Probably in the field of surgery is the operative indication so obvious as in patient with intracranial hematoma. A careful preoperative diagnosis of the nature and the site of the lesion is a prerequisite for an effective treatment. Clinically the patient's state of consciousness is the main guide in determining whether the patient should be operated on or not. Skull fracture, neurological signs, pulse rate and blood pressure readings are of minor importance in deciding whether a craniotomy is to be performed. A patient whose consciousness is returning should not be operated upon notwithstanding neurological signs show pulse increase and blood pressure rise on the presence of a depressed skull fracture as revealed by x-ray examination.

Increasing drowsiness frequently combined with motor restlessness, pupal and small pupils, which does not exceed during dehydration, present less operative indication. This lesion on the basis of clinical findings presupposes a meticulous vigilance on the part of the nursing staff and the doctor, with observation of changes in the state of consciousness in the clinical action.

The diagnostic possibilities such patient refer generally from (1) extradural hematoma (2) subdural hematoma (3) intracerebral hematoma, and (4) contusion and laceration with cerebral edema. Considerations of these are frequently met with and add to the difficulties. The significant free fluid angiography as an aid and supplement to the clinical work can hardly be overestimated at the sample which must be presented later will show. In acute head injuries pneumoencephalography is usually contraindicated from the fact that serious reactions have been observed.

When a patient is admitted with a head injury the following questions must be considered:

1. Is the unconsciousness the impaired consciousness due to an intracranial injury or to another cause?
2. What is the nature of the intracranial lesion?
3. Where is the location of the lesion—th focal lesions?
4. Is craniotomy indicated?
5. What kind of operation should be performed?

1. It is easy to quote examples of case histories related to the first question but I shall mention only the following:

A woman, B. H. aged 67 years, was admitted to Oslo City Hospital Third Surgical Department in March, 1941. She had for the past four months shown symptoms of senile dementia. It was also stated that she had been taking bromides for several weeks before admission. There was obviously head injury with fracture in the right temporoparietal region and the clinical signs made diagnosis of extradural or subdural hematoma quite possible. The content of sodium bromide in the blood, however, was 440 mg per 100. The percutaneous arteriography was not quite unequivocal and it was therefore decided to do craniotomy. A hematoma was not found. There was marked trophy of the cerebral cortex. A subarachnoid cyst containing about 50 c.c. of clear fluid was emptied. The bromide intoxication was also treated with saline solution and desoxyacetic acid. The recovery was unsuccessful, but she died several weeks later in the convalescent department, of pneumonia. The post-mortem examination did not reveal any findings of interest except those already mentioned.

The usual chronic brain disease (senile dementia, arterio-sclerosis, cerebral syphilis), acute or chronic intoxications (for example, alcohol) and head injury are frequently met with in different combinations. In this material the significance of alcohol is illustrated, one third of the patients being more or less intoxicated on admission.

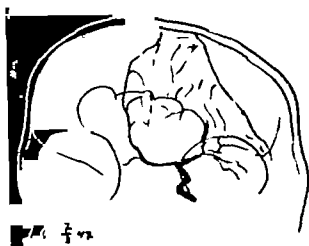


Fig. 1—J. M. Subdural hematoma. Lack of contrast between skull and surface of brain, anterior cerebral artery the right.

and 3. If it is established that the head injury is the cause of the unconsciousness, then the nature of the intracranial lesion must be ascertained. Among the diagnostic aids at our disposal the percutaneous carotid angiography is found most useful, although the technique may present some difficulties owing to the motor restlessness that often characterizes these patients. Over a period of several years, no serious complications have arisen from using this method in neurological and neuro-surgical diseases. The contrast agent is a 3 per cent solution of diodrast. For technical details see Kristiansen (1941) and Engset and Kristiansen (in press). The focal diagnosis and the question of the extent



Fig 2



Fig 3

Figs. 2 and 3—J. M. Subdural hematoma. Arteriography fourteen days after operation. Arteriogram shows still marked dislocation of anterior cerebral artery. The phlebogram in Fig 3 (same injection as Fig 2, exposure 2 seconds later) demonstrates that the cavity had decreased in size.

PL 37



Fig. 1—2 M. Thibodeau at one week after operation the brain has expanded further

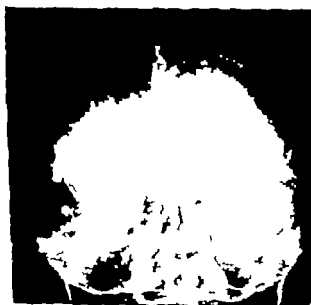


Fig. 2—3 M. Thibodeau three weeks postoperatively the expansion of the brain is complete.

sion of the lesion may also be settled by angiography although certain reservations will have to be kept in mind, as will be illustrated later.

The first case to be reported is that of a patient with an ordinary subdural hematoma.

A man, J. M. (aged 34 years) admitted to one of the medical departments of Ohio State Hospital on March 3, 1947 with diagnosis of cerebral abscess and drowsiness. He had sustained head injury in December 1946 and another head injury few days before admission to the hospital. With tentative diagnosis of subdural hematoma he was transferred to the Third Surgical Department. A percutaneous angiography on the left side showed the lateral picture of subdural hematoma with lack of contrast between the brain and the skull, and displacement of the anterior cerebral artery to the opposite side (Fig. 1).

The hematoma was evacuated through small craniotomy and the patient recovered rapidly. During the convalescence I performed repeated angiographies at five week intervals between each one. The regression of the hematoma cavity and of the displacement of the anterior cerebral artery demonstrated in Figs. 2, 3, 4, and 5.

The last angiograph (Fig. 5) done in the middle of June 1947 and shows that the artery had disappeared and that there remained only small shift of the anterior cerebral artery to the right.

The next patient represented an unusual combination of a head injury with extradural hematoma, and an intracranial tumor. He died without having been operated upon.

A man, H. T. (aged 63 years) hit by a car on Nov. 11, 1946, and was admitted to the Third Surgical Department immediately afterward with history of short period of unconsciousness and retrograde amnesia. He had fracture in the left cephalic region. On admission he was cooperative but the next day he became drowsy and later comatose. In the meantime it had been revealed that the patient had been in the hospital in 1941 with diagnosis of pituitary tumor but had refused operation on account of the fact that his brother. The brother had also had pituitary tumor and had been operated upon in 1941. He died the day after operation because of postoperative extradural hematoma.

The sequence of events in the case of this patient followed the diagnosis of traumatic subdural hematoma. The percutaneous arteriography however showed the anterior cerebral artery markedly displaced to the same side, forming the same bar outline of pituitary tumor of about the size of goose egg (Figs. 6 and 7).

The autopsy revealed large pituitary mass with recent hemorrhage in its core. The central part of the middle and lower are completely destroyed by the tumor growth. Between the base of the skull and the mass there are direct communications. In addition, the post mortem examination also revealed an extradural hematoma in the left posterior fossa (Figs. 8 and 9).

It is not possible to decide whether the intracranial hemorrhage with evacuation of the extradural clot would have saved this patient's life. But the case demonstrates a diagnostic rule that has been followed in other cases also. If a clinical diagnosis of extradural hematoma is made and the carotid angiography proves negative then a burr hole should be made in the posterior fossa in a position corresponding to the occipital pole. The extradural hematoma is not as a rule confined to the posterior fossa exclusively but will also cover little of the occipital lobe.

Reports on three cases of acute traumatic intracranial hematomas follow.

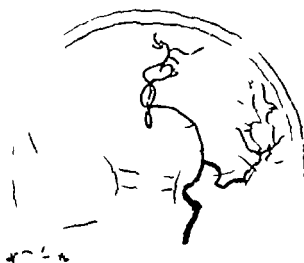


Fig. 1



Fig. 2

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Figs. 1 and 2. T. 15th day, upper lateral brain area. Note curved dislocation of anterior cerebral artery both in an anteroposterior and lateral plane.



sion of the lesion may also be settled by angiography although certain reservations will have to be kept in mind, as will be illustrated later.

The first case to be reported is that of a patient with an ordinary subdural hematoma.

A man, J. M., age 34 years, admitted to one of the medical departments of Oslo City Hospital on March 1, 1947, with diagnosis of convulsions and drowsiness. He had sustained head injury in December 1946, and another head injury a few days before admission to the hospital. With tentative diagnosis of subdural hematoma he was transferred to the Third Surgical Department. A postoperative angiography on the left side showed the lower portion of the left hemisphere with thickening of contrast between the brain and the skull, and displacement of the anterior cerebral artery to the opposite side (Fig. 1).

The hematoma was evacuated through a small craniotomy, and the patient recovered rapidly. During the convalescence I performed repeated angiographies on the same side internal to the first one. The regression of the hematoma cavity and of the displacement of the anterior cerebral artery is demonstrated in Figs. 2, 3, 4 and 5.

The first angiography (Fig. 3) as done in the middle of June 1947, and shows that the contrast had disappeared and that there remained only a small shift of the anterior cerebral artery to the right.

The next patient presented an unusual combination of a head injury with extradural hematoma, and an intracranial tumor. He died without having been operated upon.

A man, H. T., age 63 years, was brought on Nov. 11, 1946, and admitted to the Third Surgical Department immediately after a fall. He does not recall period of unconsciousness and retrograde amnesia. He had fracture in the left occipital region. On admission he was comatose, but the next day he became lucid. At that time it had been revealed that the patient had been in the hospital 1942 with diagnosis of pituitary tumor but had refused operation on account of the size of his brother. The brother had also had pituitary tumor and had been operated upon 11 years before the patient's operation because of postoperative intracranial hematoma.

The sequence of events in the case of this patient from the diagnosis of an extradural hematoma. The postoperative angiography, however, showed the anterior cerebral artery markedly displaced to the same side forming the same results as in pituitary tumor of about the size of goose egg (Fig. 6 and 7).

Thus, the stereogram did not confirm the clinical diagnosis of an extradural hematoma. The conclusion was that he probably had hemorrhages of traumatic origin in the tumor, which regarded as inoperable. He died some hours later in comatose condition.

The autopsy revealed large pituitary tumor (the rest of the brain was normal). The central part of the middle cranial fossa were completely destroyed by the tumor growth. Distension of the brain of the skull and the brain were increased. The posterior horns of the lateral ventricles had an extradural hematoma beneath the posterior horns (Fig. 8 and 9).

It is not possible to decide whether a craniotomy with evacuation of the extradural clot would have saved this patient's life. But the case demonstrates a diagnostic rule that has been of value in other cases too. If a clinical diagnosis proves negative, a craniotomy with evacuation of the extradural clot is not as a rule confined to the posterior fossa and tentorium but will involve a little of the occipital lobe.

Reports on three cases of a uterine malformation of the uterine horns follow.

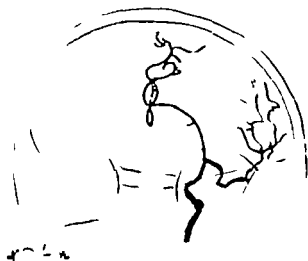


Fig 6



Fig 7

Figs 6 and 7—II T. Intracranial tumor, radical brain tumor. Not, mixed dislocation of anterior cerebral artery both in of regenerative and lateral

tion of the lesion may also be settled by angiography although certain reservations will have to be kept in mind as will be illustrated later.

The first case to be reported is that of a patient with an ordinary subdural hematoma.

A man, J. M., aged 34 years, admitted to one of the medical departments of Oslo St. Hospital March 4, 1944 with diagnosis of concussion and drowsiness. He had sustained head injury in December 1943, and another head injury few days before admission to the hospital. With tentative diagnosis of subdural hematoma he was transferred to the Third Surgical Department. A preoperative angiogram on the left side showed the lateral picture of a bilateral hematoma with lack of contrast between the brain and the skull, and displacement of the anterior cerebral artery to the opposite side (Fig. 1).

The hematoma was evacuated through a small craniotomy and the patient recovered rapidly. During the convalescence I performed repeated angiographies with few week intervals but each one. The regression of the hematoma cavity and of the displacement of the anterior cerebral artery is demonstrated in Figs. 2, 3, 4 and 5.

The last angiography (Fig. 5) is done in the middle of June 1944 and shows that the artery had disappeared and that there remained only a small shift of the anterior cerebral artery to the right.

The next patient presented an unusual combination of a head injury with extradural hematoma and an intracranial tumor. He died without having been operated upon.

A man, H. T., aged 33 years, was hit on Nov. 11, 1943, and was admitted to the Third Surgical Department immediately afterwards with history of short period of unconsciousness and retrograde amnesia. He had fracture in the left occipital region. On admission he was cooperative but the next day he became drowsy and later semicomatose. The neurosurgeon had been consulted but the patient had been in the hospital since 1942. He had now a history of pituitary tumor but had refused operation on account of the illness of his brother. The brother had also had a pituitary tumor and had been operated upon in 1931. He died the day after operation because of postoperative extradural hematoma.

The sequence of events in the case of this patient favored the diagnosis of traumatic extradural hematoma. The postoperative roentgen picture, however, showed the anterior cerebral artery markedly displaced to the side while forming the arch in the sulcus of the pituitary fossa of the base of the skull (Figs. 6 and 7).

Thus the roentgenogram did not confirm the clinical diagnosis of an extradural hematoma. The conclusion is that he probably had hemorrhages of traumatic origin in the tumor which regarded as inoperable. He died some hours later he was very comatose.

The autopsy revealed a large pituitary tumor. The recent hemorrhages into the tumor were seen. The central parts of the middle cranial fossa were completely destroyed by the tumor growth. Between the base of the skull and the sella by there were direct communications. In addition, the post mortem examination revealed an extradural hematoma in the left posterior fossa (Figs. 8 and 9).

It is not possible to decide whether or not an anterior wall excision of the extradural loc would have saved this patient's life. But the well-known contrast is a diagnostic rule that has been of value in other cases also. In a clinical diagnosis of extradural hematoma: male and the roentgenography; if necessary then a burr hole should be made in the posterior fossa or in position corresponding to the occipital pole. The extradural hematoma is not as a rule confined to the posterior fossa unless it will also encroach a little of the occipital lobe.

Reports on three cases of traumatic intracerebral hematomas follow.





Fig. 8-11. T. Death section showing large pineal tumor and several hemorrhages.



FIG. 8-12. T. Extracranial clot in left posterior horn destruction of central part of middle cerebral lobe.

A man, B. A. aged 5 years, was admitted to the Third Surgical Department of Oslo City Hospital on Sept 7 1940, after fall from high place. He was unconscious restless and ray examination showed fracture in the right temporal bone. Due to technical failure in the ray machine an attempt to do art angiography was unsuccessful.

A subtemporal burr hole made on the right side corresponded to the site of the fracture, but no extradural or subdural clot was found. As the patient's condition deteriorated after some hours, left-sided craniotomy was performed. A subdural hematoma of fairly large size was found and evacuated. The operation however had no effect; he remained unconscious and died in peripheral peritonitis the next morning.

Post mortem examination revealed the fracture of the right temporal bone. The subdural hematoma on the left side had been completely removed at the operation and there were no signs of superficial cerebral contusion. After fixation of the brain as usual, and examination of the gross sections revealed a large hematoma in the left temporal lobe (Fig 10).



FIG. 10.—Intracerebral hematoma in left temporal lobe.

The intracerebral damage was undoubtedly the cause of this patient's death. The hyperthermia may be explained as the result of pressure from the hematoma on the central part of the brain. Without angiography it is hardly possible to diagnose this combination of extracerebral and intracerebral hematomas. This case also demonstrates that a skull fracture is not invariably situated on the same side as the intracranial hematoma.

Traumatic intracerebral hematomas of the kind described here are usually regarded as inoperable. There are however frequent reports of successful removal of large intracerebral hematomas which have been operated upon as a result of faulty diagnoses of intracranial tumors.

I think it is incorrect to regard the acute traumatic intracerebral hematomas of the so-called closed head injuries as unsuitable for operation. If the hematoma is located in a region where it can be reached by a small craniotomy and

If it can be localized angiographically I feel that such lesions are very amenable to operative therapy. The following two cases demonstrate the truth of this point of view.

A man, E. K., aged 56 years, admitted to hospital just outside Odo after being hit by a car Nov. 27, 1916. Due to increasing drowsiness and left-sided hemiparesis, he was transferred seven days later to the Third Surgical Department of Odo City Hospital.

A percutaneous cerebral angiography on the right side showed very marked distortion of the anterior cerebral artery to the left and exceptional elevation of the Sylvian group (Fig. 11).

A diagnosis of subdural hematoma combined with intracerebral hematoma in the right temporal lobe was made and a small subtemporal craniotomy was performed. A subdural hematoma of about 1 cm. thickness removed by suction. Medially is that, in the temporal lobe, large hematoma as found containing mainly clotted blood. The diameter of this intracerebral hematoma 3 cm. After evacuation of the hematoma and complete hemostasis the wound was closed and the patient recovered rapidly.

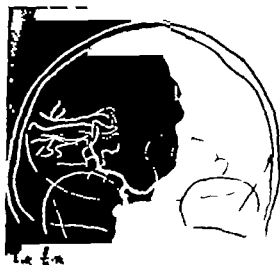


Fig. 11—E. K. Subdural, intracerebral hematoma. Marked distortion to left of anterior cerebral artery and less than of Sylvian group. Wound line displaced medially.

Percutaneous carotid angiography during the postoperative course. In some cases lateral but even each angiography showed the regression of the lateral findings (Figs. 1 and 13). Fig. 1, demonstrates also the beautiful bilateral filling of the carotid system which is obtained when the contralateral common carotid artery is compressed during its rejection of contrast. The normally latent anastomosis in the circle of Willis opens retrogradely when the blood flow in one carotid artery is stopped. This bilateral filling is of importance if there is doubt as to the occurrence of unilateral or bilateral subdural hematomas.

The other patient, E. J. was a 50-year-old man admitted to the Third Surgical Department on Dec. 2, 1916, after head injury. During the next five days he became drowsy and developed paresis of the left facial nerve and the left arm. The angiography revealed an archlike elevation of the middle cerebral artery suggesting an expansive process in the right temporal lobe (Figs. 14 and 15).



Fig. 12—P. L. Arteriogram eleven days after operation. Bilateral filling branches and compression of contralateral carotid artery during contrast injection into right carotid as other artery. Dislocation less pronounced.

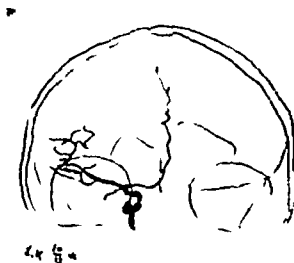


Fig. 13—P. L. Arteriogram one week after operation. Arterial system still visible and at least some of arteries



If it can be localized angiographically I feel that such lesions are very well amenable to operative therapy. The following two cases demonstrate the truth of this point of view.

A man, E. K., aged 65 years, was admitted to hospital just outside Oslo after being hit by car Nov 27 1944. Due to increasing drowsiness and left-sided hemiparesis, he was transferred seven days later to the Third Surgical Department of Oslo City Hospital.

A percutaneous cerebral angiography on the right side showed very marked displacement of the internal cerebral artery to the left and an exceptional elevation of the Bittman group (Fig. 11).

A diagnosis of an intracerebral

temporal lobe

hematoma of

parietal lobe is

this intracerebral

hematoma the skull was opened and the patient recovered rapidly.

After evacuation of the hematoma, all complete



Fig. 11—E. K. Subtotal in cerebral hematoma. Marked displacement to left of anterior cerebral artery and elevation of Bittman group.

Percutaneous cerebral angiography during the postoperative course in some weeks (interval between each angiography) shows the regression of the abnormal findings (Figs. 12 and 13). Fig. 12 demonstrates the complete lateral filling of the carotid in the

back is added when the contralateral common carotid artery is compressed during the injection of contrast. The normally is not anastomosis the circle of Willis opens further towards when the blood flow in one carotid artery is stopped. This bilateral filling is of importance if there is doubt to be overcome of unilateral or bilateral unilateral hematomas.

The other patient E. J. was a man aged 54 years who was admitted to the Third Surgical Department on Dec 1 1944, after head injury. Two or three days he became drowsy and developed paresis of the left facial nerve and the left arm. The angiography revealed an arachnoid lesion of the middle cerebral artery suggesting aneurysm in the right temporal lobe (Figs. 14 and 15).

A traumatic hematoma in the right temporal lobe was diagnosed, and a small craniotomy performed six days after the injury localized subdural hematoma which was removed. Mainly it was that there was intracerebral hematoma in the temporal lobe containing clotted blood and lacerated brain tissue and the hematoma was evacuated. The patient's condition improved rapidly. A second stereogram on the day of discharge one month after admission gave normal picture of the intracranial vessels (Fig. 16).

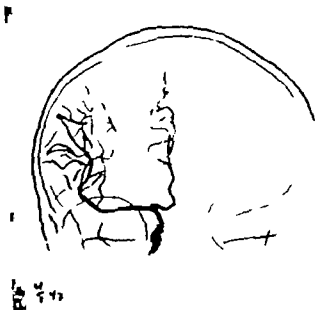


Fig. 16—P. J. Normal stereogram four weeks after operation.

These last two cases give a demonstration of the value of percutaneous cerebral angiography in acute head injuries, particularly when one is confronted with the case presenting the same kind of lesion which proved fatal. If a pre-operative angiograph had been successful in that case also, that patient too might have been saved.

All three cases show a combination of a relatively localized subdural hematoma and an intracerebral hematoma in the temporal lobe. The hematomas are probably due to a small cortical contusion with laceration of cortical vessel which give hemorrhage partly outward into the meninges, partly inward into the cerebral substance. The rather protracted course in the two last mentioned patients may perhaps be a result of the hemorrhage occurring at intervals and not immediately following the injury (Hollinger 1891).

The excellent result of operative treatment on the firm of intracerebral hematomas is a temptation to apply a similar ray to a number of cases of ordinary brain hemorrhages and apoplexies. Such attempts have been made previously by Penfield (1933) among others. I have tried such procedure in one patient after localization of the hemorrhage by percutaneous angiography. The result was not encouraging in that case due to the fact that the meningeal hem-

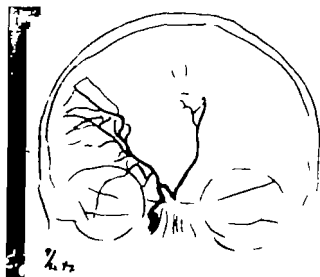


Fig. 14—M. J. Medial view of the brain. Disposition of anterior cerebral artery is left very marked elevation of left hemisphere.

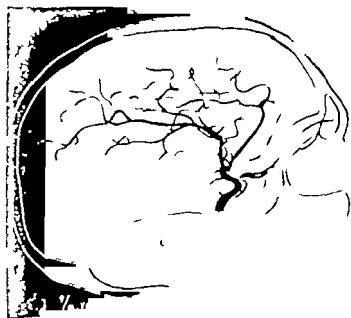


Fig. 15—L. J. Lateral view of the brain. Disposition of anterior cerebral artery is left very marked elevation of left hemisphere.

A traumatic hematoma in the right temporal lobe as diagnosed and small craniotomy performed six days after the injury showed localized subdural hematoma which removed Medulla & that there intracerebral hematoma the temporal lobe containing lotted blood and lacerated brain tissue with hematoma evacuated. The patient condition improved rapidly. Another arteriogram on the day of discharge one month after discharge gave normal picture of the intracranial vessels (Fig 16).

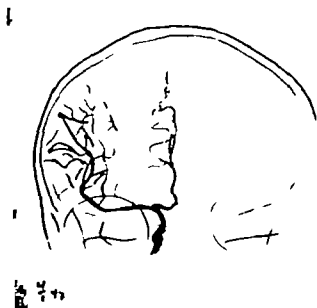


Fig 16—F. J. Normal arteriogram four weeks after operation.

These last two cases give a demonstration of the value of percutaneous cerebral angiography in acute head injuries, particularly when one is confronted with the case presenting the same kind of lesion which proved fatal. If a pre-operative angiography had been successful in that case also that patient too might have been saved.

All three cases show a combination of a relatively localized subdural hematoma and an intracerebral hematoma in the temporal lobe. The hematomas are probably due to a small cortical contusion with laceration of cortical vessels which give hemorrhage partly outward into the meninges, partly inward into the cerebral substance. The rather protracted course in the two last mentioned patients may perhaps favor a theory of the hemorrhage occurring at intervals and not immediately following the injury (Bollinger 1891).

The excellent result of operative treatment on this form of intracerebral hematoma is a temptation to apply a similar therapy in suitable cases of ordinary head injury. The results are not encouraging in that case due to the fact that the mass of blood

rhage in the frontal lobe had ruptured into the lateral ventricle. Evacuation of the hematoma had no influence on the patient's condition. Other cases may prove more successful.

4 The fourth question to be answered in cases of head injuries, that is, whether there is indication for operative treatment or not, I have touched on repeatedly in the previous pages. There is a need to stress the point that the patient's state of consciousness and the changes in that state are the main clinical features to be observed.

It has been said that the results of treatment of craniocerebral lesions can never be satisfactory if the surgeon is not lying with his patients. Everyone who has been engaged in that field of surgery will confirm this view. But as this ideal demand cannot possibly be realized, the value of simple principles of observation both for interns, residents, and nursing staff cannot be overestimated. That simplicity may be attained if every sign indicating clouding of the patient's consciousness is reported at once.

In dubious cases the percutaneous cerebral angiography is completely devoid of danger and affords the necessary diagnostic aid.

5 The last question, that of the operative technique, has also been mentioned previously. The craniotomy in acute head injuries should be performed as a burr hole with nibbling off of the edges until the hole is just sufficiently large to remove the hematoma by suction and to stop bleeding points. Osteoplastic craniotomies should never be performed in acute head injuries as they only add another serious trauma to the original damage. Useless exploratory burr holes in different parts of the skull may be avoided through meticulous neurological examination and preoperative percutaneous cerebral angiography with Diodrast.

#### SUMMARY

The percutaneous cerebral angiography has proved a valuable diagnostic aid in patient with acute head injuries. Case histories are reported showing the different diagnostic problems occurring in such patients during the first days after the accident. Special attention is given to the combination of subdural and intracerebral hematomas. Without cerebral angiography the presence of the intracerebral clot will easily be overlooked.

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Ortberg, Conrad

# END RESULTS IN THE TREATMENT OF CANCER OF THE STOMACH

## ANALYSIS OF SEVEN HUNDRED NINETY FIVE CASES

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CANCER of the stomach is the most common and one of the most rapidly fatal of all malignant tumors. As a result there is not only an understandable pessimism concerning the curability of this disease but also no hope whatsoever in the minds of the vast majority. Many of our most prominent surgeons, busily engaged in performing operations on the gastrointestinal tract for cancer have made the statement, both privately and in public, that they have never seen a five-year survival from gastrectomy for carcinoma of the stomach. If such views are widely entertained by the specialist the physician in general practice can hardly be expected to search very eagerly for early cancer of the stomach. In the first place the most logical question might be: Is it possible to recognize gastric cancer in an early curable stage? Can this experience be repeated often enough to warrant continued watchfulness on our part in the hope of discovering the presence of the disease before it has passed beyond all hope of cure?

Before an attempt is made to answer these questions the symptomatology of gastric cancer might be reviewed. Simple indigestion is probably the most dangerous complaint of an person in middle or late life. Because it is like wise the most common little attention is paid to the vague but portentous beginnings of what may prove to be a fatal disease. Yet frequently the warning of something amiss, some aberration from the normal is given in plenty of time if only the patient and the physician were more alert.

Nausea, vomiting, anorexia, emaciation, palpable supraclavicular lymph nodes, and a large gastric mass are all gastric cancer in capital letters, but with slight fulness, alternating tendency toward constipation and a few pound loss in weight. More frequently than not the supposed ulcer syndrome appearing for the first time in a person past 40 years of age has dashed the goal for a small relatively slow growing ulcerating cancer in a favorable setting. Little practical there is that the patient has cancer of the stomach, and if he is not told he will think the ulcer to be gastric and not duodenal. Every effort should be made to remove the lesion as soon as possible.

Many patients are treated for anemia without secret using the cause of that anemia. The first phenomenon to be the first and only symptom of chronic bleeding is pallor of the face. Many such patient have received digital instead of gastrointestinal ray series.

Probably the chief symptom of gastric cancer is awareness that all is not just right though fit the patient cannot say where why for the

Read before the New York Academy of Medicine, New York, N. Y., February 14, 1934.

first time in his life he may become conscious of a protracted change in his sense of well being; he may be aware of his stomach (stomach consciousness) where before he did not know it existed. He may not have cancer of the stomach, but only an inadequately conducted gastrointestinal x ray series and fluoroscopy after barium swallowing, supervised by a competent radiologist will settle the question. A patient is seldom annoyed when told he does not have a serious gastric disorder.

Once a diagnosis of cancer of the stomach is established, is any useful purpose served by subjecting the patient to laparotomy with the hope of performing either partial or complete gastrectomy? It is our considered opinion that the hope for cure is a very definite one which should be offered all such patients, in greater numbers as each year goes by. In order that we may appreciate the change in our concepts concerning the outlook in cancer of the stomach, let us examine the material at a large clinic in New York City studied over a period of thirty years.

#### MATERIAL FOR STUDY

From 1916 through 1941 79 patients suffering from gastric cancer were examined and treated at the Memorial Hospital for Cancer and Allied Diseases. Of that entire number only 26 or 34 per cent survived for a five year period without recurrence after subtotal gastrectomy. This curability rate of 34 per cent is not a fair valuation of the prospect today because it includes the early history of the hospital as far back as 1916 and is based on a resectability rate which is only slightly higher, namely 10 per cent (Table I). Five of the patients operated on prior to 1936 were living and well for more than ten years. At first glance this bare statement of fact appears gloomy indeed. Almost forcing us to conclude that we have been wasting our time and many thousands of dollars in attempting to cure patients of a disease which is almost invariably fatal. Yet life has been precious to those twenty or so people who have no great interest in statistics or what happened to all the others. Upon closer scrutiny of the material, we readily observe a very remarkable change in the method of management of cancer of the stomach. Palliative operations were common and resections were rarely performed in the earlier decade now the reverse is true. This change has been accompanied by a remarkable upward trend in the cure curve of end results.

TABLE I FIVE YEAR SURVIVAL FOLLOWING RESECTION FOR GASTRIC CANCER, FROM 1916 THROUGH 1941

TYPE OF	TOTAL CASES	FIVE YEAR SURVIVAL	
		NUMBER	PER CENT
Total patients with gastric cancer	79	26	34
Number surviving gastrectomy	79	26	34.7

#### THE EARLY TABILITY OF GASTRIC CANCER

From 1916 until 1930, of 97 patients who were seen in our clinic only 8, or 9 per cent had resectable gastric cancers. At that time became evident that there was obvious need for segregating such patients in a special clinic

devoted to tumors of the stomach, the resectability rate increased to 77 per cent during the years of 1931 through 1936 and 26 per cent for the years of 1937 through 1941. In a far shorter period more patients were seen, and that is more important a greater number of resection was performed. Where as only one of the few patients undergoing gastrectomy before 1931 survived for a five year period, an increasingly large number was now being offered the chance of cure. Within the last eight years techniques of two operative procedures became more widely employed and were standardized in clinics throughout the world. We refer to (a) the procedure known as total or complete gastrectomy and (b) transstomachic resection of the gastric cardia. Greater understanding of preoperative and postoperative care and advances in anesthesiology made these operations less hazardous and part of the armamentarium of

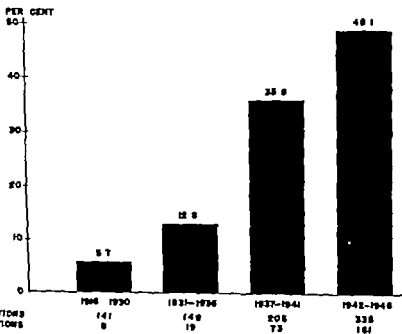


Fig. 1—The resectability of stomach cancer. The time service of the Memorial Hospital, New York, N. Y. from 1906 through 1946.

many gastric surgeons. As a result no longer was a cancer of the stomach not resectable as long as the disease was confined to that organ and adjacent lymph nodes and not fixed to structures whose removal might not be compatible with life. It now was that in the years 1942 through 1946 not only were there many more patients treated than in the previous five year period, but also the resectability rate soared to 48.1 per cent. In fact 48.1 per cent of all patients submitted to laparotomy underwent the subtotal or total gastrectomy and 6 per cent were operated on for palliative curative purposes (Table II). Thus for a large number of patients a given a chance to live.



first time in his life he may become conscious of a protracted change in his sense of well-being; he may be aware of his stomach (stomach consciousness) where before he did not know it existed. He may not have cancer of the stomach, but only an adequately conducted gastrointestinal x-ray series and fluoroscopy after barium swallowing, supervised by a competent radiologist will settle the question. A patient is seldom annoyed when told he does not have a serious gastric disorder.

Once a diagnosis of cancer of the stomach is established, is an useful purpose served by subjecting the patient to laparotomy with the hope of performing either partial or complete gastrectomy? It is our considered opinion that the hope for cure is a very definite one which should be offered all such patients, in greater numbers as each year goes by. In order that we may appreciate the change in our concepts concerning the outlook in cancer of the stomach let us examine the material at a large clinic in New York City studied over a period of thirty years.

#### MATERIAL FOR STUDY

From 1916 through 1941 703 patients suffering from gastric cancer were examined and treated at the Memorial Hospital for Cancer and Allied Diseases. Of that entire number only 28 or 3.4 per cent survived for a five year period without recurrence after subtotal gastrectomy. This curability rate of 3.4 per cent is not a fair evaluation of the prospect today because it includes the early history of the hospital as far back as 1916, and is based on a resectability rate which is only slightly higher, namely 10 per cent (Table I). Five of the patients operated on prior to 1938 were living and well for more than ten years. At first glance this late statement of effect appears gloomy indeed, almost forcing us to conclude that we have been wasting our time and many thousands of dollars in attempting to cure patients of a disease which is almost invariably fatal. Yet life has been precious to those twenty-six people who have no great interest in statistics or what happened to all the others. Upon close scrutiny of the material we readily observe a very remarkable change in the method of management of cancer of the stomach. Palliative operations were common and resection were rarely performed in the earlier decade; now the reverse is true. This change has been accompanied by a remarkable upward trend in the cure curve of end result.

TABLE I. FIVE YEAR SURVIVAL FOLLOWING RESECTION FOR GASTRIC CANCER FROM 1916 THROUGH 1941

TYPE OF STOMACH	TOTAL	FIVE YEAR SURVIVAL	
		NUMBER	PER CENT
Total patients with gastric cancer	703	28	3.4
Number surviving gastrectomy	78	26	31.7

#### THE RESECTABILITY OF GASTRIC CANCER

From 1916 until 1930 of 27 patients who were seen in our clinic only 8, or 29 per cent had resectable gastric cancer. As it later became evident that there was obvious need for segregating such patients in a special clinic

TABLE III OPERATIVE MORTALITY FROM ALL OPERATIONS FOR GASTRIC CANCER, FROM 1910 THROUGH 1916

TYPE OF OPERATION						
All operations						
Exploratory operation	1		8.8	43	6	11.6
Palliative operation	7	7	7.3	61	6	9.8
Resection	8	8	62.3	19	6	31.6
Subtotal resection	8	8	6.8	19	6	37.3
Removal of the card				1	0	0.0
Total gastrectomy						
	1917 through 1941			1912 through 1916		
All operations	167	31	18.	375	57	17.0
Exploratory operation	57	6	10.5	104	3	5.0
Palliative operation	67	11	16.4	4	17	23.0
Resection	3	14	19	161	35	1.1
Subtotal resection	5	9	13.5	0	9	8.8
Removal of the card	0		0.0	14	14	14.0
Total gastrectomy	10	1	24.0	77	1	34.4

test of critical statistical analysis, the reason being that the minimum and maximum duration are too widely separated. The average duration of preoperative symptoms for 9.7 months obtains fairly evenly both for the patients who survived five years without recurrence and for those who died of recurrent cancer in a shorter period (Table IV). We had previously entertained the clinical impression that the patients whose preoperative duration of symptoms was short very frequently presented inoperable cancers at laparotomy and conversely we had observed that some patients with a long history still had cancers readily removable. Two of these patients in the five-year group were more than 10 years long at the time of gastric resection.

TABLE IV PRE-OPERATIVE DURATION OF SYMPTOMS IN RELATION TO PERCENTAGE SURVIVAL FOR GASTRIC CANCER, FROM 1910 THROUGH 1916

PRE-OPERATIVE DURATION OF SYMPTOMS (MONTHS)		PERCENTAGE SURVIVAL	
Less than 6	6 or more	Survived 5 years or more	Died of recurrent cancer
10	14	4	7
10	14	4	7

Does the Histologic Type of Tumor Have Any Bearing on Ultimate Prognosis? We had anticipated a higher percentage of long-term survivors in patients with gastric cancer of the polypoid exophytic type. Of nineteen patients with such tumors, only 5 lived without recurrence for more than 5 years subsequent to gastrectomy (26.3 per cent). On the other hand, one-third of our patients with ulcerating gastric cancers who survived resection attained definite cures (33.9 per cent). The prognosis for anular cancers, contrary to our previous conclusion, is less optimistic as well. And now that these cancers have usually been localized in the time survival interval is done (22 per cent). One-quarter of all infiltrating gastric cancers removed surgically are apparently completely controlled, as judged by the survival rate of these patients (25 per cent). Carcinomas in situ the miniature focal can-

TABLE II OPERABILITY AND RESECTABILITY OF GASTRIC CANCER, FROM 1921 THROUGH 1946

PERIOD	TOTAL	OPERABILITY		RESECTABILITY	
		PER CENT OF		PER CENT OF OPERABLE CASES	PER CENT OF TOTAL CASES
1916 to				87	26
1931 to				1.8	7.7
1937 to				33.8	7.7
1945 to 1				49.1	29.8

Significantly 34.7 per cent of the 75 survivors of resection lived for five years without evidence of recurrence. It is too early as yet to evaluate the end results of treatment in the years 1941 through 1946, but it seems logical to believe that a far greater number of patients will have been offered a chance to survive for many years as a direct result of the increase in the resectability rate and lowered operative mortality.

#### THE OPERATIVE MORTALITY FOR CANCER OF THE STOMACH

Does the increase in the resectability rate for gastric cancer carry with it an unjustified hazard? Here we encounter what, at first glance, may be considered as conflicting results. In the early period from 1916 through 1930 five of eight patients undergoing gastric resection did not survive the operation. The operative mortality declined from 62.5 per cent to 31.8 per cent during the next five years. Yet, the truly gratifying improvement by 1941 of 19 per cent did not appear to continue during the last five-year period (41.7 per cent). This seeming paradox in spite of the newer advances in pre- and postoperative care and anesthesiology is explained by various factors. Having extended the scope of subtotal gastrectomy to its fullest degree surgeons realized more fully that every attempt must be made to remove a cancerous stomach wherever possible. The techniques of total gastrectomy and transthoracic resection of the gastric cardia were, therefore, applied with ever increasing frequency. Obviously a greater operative hazard had to be faced, as both these procedures carry a high operative mortality and this figure is included with the over-all mortality rate for gastric resections of all types. Furthermore during the last five years at the Memorial Hospital 4.8 per cent of all gastric resections for cancer are of this major character, namely total gastrectomy and transthoracic cardectomy (Table III). Of ninety-two subtotal gastrectomies for cancer (1941 through 1946) there were only nine operative deaths, or 9.8 per cent. It must never be forgotten, however, that if a gastric cancer is not resected, the patient invariably dies. Here again it is too early to evaluate the end results obtained by such major operations as total gastrectomy and transthoracic cardectomy but over eighty persons have been given an opportunity for life which could not possibly have been otherwise afforded.

#### FACTORS WHICH INFLUENCE THE END RESULTS: THE TREATMENT OF GASTRIC CANCER

*Duration of Symptom.* Platnick and Pyle<sup>1</sup> state that following their review for Gastric Cancer—The application of the factor does not pass the

TABLE VI. MICROSCOPIC ILLUSTRATION OF GASTRIC CANCER IN RELATION TO OVER FIVE YEAR SURVIVAL (METASTASIS TO REGIONAL LYMPH NODES) FROM 1916 THROUGH 1941

HISTOLOGIC PATTERN	ALL IV TO IFA THAN FIVE YRS			SURVIVAL OF FIVE YEARS OR MORE		
	TO ALL YRS	WITH OD L METAS YRS	WITH LT LOCAL MET YRS	TOT YRS	WITH OD MET STAGES	WITHOUT OD MET YRS
Total	4	3	4	20	4	3
Intralobular adenocarcinoma	4	3	1			
Adenocarcinoma	29	1	1	13		13
Adenocarcinoma with glandular features	7	1	6	1		1
Adenocarcinoma with nodular proliferation		4	4		8	
Adenocarcinoma (high grade) with features and nodular proliferation				1		1
Lymphoma	1	1				

*The Microscopic Grade of Gastric Cancer* The prognosis of gastric cancer can definitely be evaluated by grouping the histologic grading of the resected tumors. If we group the total cases as charted in Table VII it will be seen that the percentage of five year survival after resection becomes progressively lower with the ascending degrees of malignancy. For example

GRADE	PER CENT OF FIVE YEAR SURVIVAL (PER CENT)	PER CENT OF FIVE YEAR SURVIVAL (PER CENT)
	100.0	0.0
Grade I	41	59.7
Grade II	20	1.0
Grade III	1	43.3

From these facts we may validly reason that patients with the relatively rare (Grade I) cancer of the stomach (total) have an extraordinarily

TABLE VII. MICROSCOPIC ILLUSTRATION OF GASTRIC CANCER BY RESECTION OVER FIVE YEARS (HISTOLOGIC GRADE OF TUMOR) FROM 1916 THROUGH 1941

HISTOLOGIC PATTERN	TUMOR	ALL IV TO IFA THAN FIVE YEARS				SURVIVAL OF FIVE YEARS OR MORE			
		TOT YRS	I	II	III	TOT YRS	I	II	III
Total		4	14	1	1	21	3	1	4
Diffuse infiltrating adenocarcinoma		4	9	17	7	13	1	7	3
Adenocarcinoma with glandular features		7	1			1	1		
Adenocarcinoma with nodular proliferation		4	4	1	3	7		3	4
Adenocarcinoma (high grade) with features and nodular proliferation						1	1		
Lymphoma		1		1					

\*The total includes four metastatic carcinomas

cer of the stomach is, of course, the most favorable or rather the least dangerous of all gastric cancers. A patient surviving partial gastrectomy for this tumor may expect a cure provided he does not succumb to another disease in the mean time (100 per cent) (Table V). An exception to this last statement may result in the instance of a patient recently treated—a 70-year-old woman who successfully underwent subtotal gastrectomy for a small antral cancer. In the specimen were found at least a dozen minute small mucosal plaques, each of which on microscopic study proved to be carcinoma *in situ*. No one knows the time it would take for any one of these tiny focal cancers to grow sufficiently to cause the symptoms and signs of gross gastric cancer. Because of the multi-

TABLE V GROSS PATHOLOGIC LESIONS IN RELATION TO OVER FIVE YEAR SURVIVAL FOLLOWING RESECTION FOR GASTRIC CANCER FROM 1916 THROUGH 1941

GROSS PATHOLOG.	ALL OPERATIVE SURVIVALS	SURVIVAL OVER 5 YEARS	SURVIVAL OF FIVE YEARS OR MORE				
			TOTAL	5-7 YR	7-9 YR	10-15 YR	15 YR
Total nos	78	49	42	14	7	4	1
Ulcerating	62	41	31	1	6	3	
Antral	2	17	5		1	2	1
Polypoid	19	14	8	1	2	2	
Infiltrating	16	13	4		3	1	
<i>In situ</i>				2			

centric origin, we naturally assume that other similar foci may be present in the residual proximal stomach. We must therefore decide whether to perform a total gastrectomy in this 70-year-old woman with the attendant risk of this operation or to watch her constantly by fluoroscopic and gastroscopic surveillance during the remainder of her life.

*Presence or Absence of Metastases Regional Lymph Nodes.*—The absence of metastatic cancer in the lymph nodes removed with the resected stomach has always been heralded as an important factor of good prognosis in the evaluation of end results, but the total number of patients surviving without recurrence for five years after resection is so small that percentage figures of no formation of only relative value. Of our patients who reached the period of definitely cure 69 per cent did not have metastases in the perigastric lymph nodes. The surprising fact is that in the remainder of our long-term survivors, the 30.8 per cent of the cured cases cancer was demonstrably present in the excised lymph nodes (Table VI). It is a truism that cancer of the stomach is not inoperable when it has passed beyond the confines of the stomach to the perigastric lymph nodes, yet this fact is often not appreciated by surgeons who refuse to perform gastrectomy because of apparently gross metastatic cancer in lymph nodes adjacent to the primary tumor. In the first place even expert pathologists frequently are in error concerning the gross appearance of cancer in lymph nodes, and in the second place such lesions if widely resected may be permanently eradicated.

The relative prognosis of patient who has undergone gastrectomy for cancer with and without metastases to regional lymph nodes may also be expressed in the following manner: (a) those without metastases to lymph nodes—42.8 per cent five-year survival (1) those with proved metastases to lymph nodes—24.2 per cent five-year survival.

TABLE VI. MICROSCOPIC PATHOLOGY OF GASTRIC CANCER IN RELATION TO OVER FIVE SURVIVAL (METASTASIS TO REGIONAL LYMPH NODES)  
FROM 1916 THROUGH 1941

HISTOLOGIC PATHOLOGY	SURVIVAL OF LESS THAN FIVE YEARS			SURVIVAL OF FIVE YEARS OR MORE		
	TOTAL CASES	WITH NO METASTASIS	WITH REGIONAL METASTASIS	TOTAL CASES	WITH NO METASTASIS	WITH REGIONAL METASTASIS
Total	49	3	4	24	9	15
Ungraded	4	3	1			
Superficial adenocarcinoma						
Adenocarcinoma	29	1	1	13		13
Adenocarcinoma with gastric mucosa features	7	1	0	1		1
Adenocarcinoma with serosal penetration		4	4		3	2
Adenocarcinoma with gastric mucosa features and serosal penetration				1		1
Lymphoplasmic	1	1				

The Microscopic Grade of Gastric Cancer—The prognosis of gastric cancer can definitely be evaluated by grouping the histologic grading of the selected tumors. If we group the total cases as charted in Table VII it will be seen that the percentage of five-year survival after resection becomes progressively lower with the ascending degrees of malignancy. For example

GRADE	SURVIVAL OF LESS THAN FIVE YEARS (PER CENT)	SURVIVAL OF FIVE YEARS OR MORE (PER CENT)
Grade I	100.0	0.0
Grade II	41.7	33.3
Grade III	30.0	70.0
Grade IV	16.7	83.3

From these facts we may deductively reason that patients with the relatively rare Grade I cancer of the stomach (scarcely) have an extraordinarily

TABLE VII. MICROSCOPIC PATHOLOGY OF GASTRIC CANCER IN RELATION TO OVER FIVE SURVIVAL (HISTOLOGIC GRADE OF TUMOR)  
FROM 1916 THROUGH 1941

HISTOLOGIC PATHOLOGY	SURVIVAL OF LESS THAN FIVE YEARS				SURVIVAL OF FIVE YEARS OR MORE					
	TOTAL CASES	I	II	III	IV	TOTAL CASES	I	II	III	IV
Total	49	14	1	10		24	0	10	13	2
Superficial adenocarcinoma										
Adenocarcinoma	29			13		13	1	7	5	
Adenocarcinoma with gastric mucosa features	7		1	6		1	1			
Adenocarcinoma with serosal penetration	8		4	1	3	7		3	4	
Adenocarcinoma with gastric mucosa features and serosal penetration						1	1			
Lymphoplasmic	1			1						

\*The total includes four ungraded carcinomas.

cer of the stomach is, of course the most favorable, or rather the least dangerous of all gastric cancers. A patient surviving partial gastrectomy for this tumor may expect a cure provided he does not succumb to another disease in the mean time (100 per cent) (Table V). An exception to this last statement may result in the instance of a patient recently treated—a 70-year-old woman who successfully underwent subtotal gastrectomy for a small antral cancer. In the specimen were found at least a dozen minute sessile mucosal plaques, each of which on microscopic study proved to be carcinoma *in situ*. No one knows the time it would take for any one of these tiny focal cancers to grow sufficiently to cause the symptoms and signs of gross gastric cancer. Because of the multi-

TABLE V GROSS PATHOLOGY IN RELATION TO OPERATIVE SURVIVAL FOLLOWING RESECTION FOR GASTRIC CANCER FROM 1918 THROUGH 1941

GROSS PATHOLOGY	ALL OPERATIVE SURVIVALS	ALL BY OTHER CASES	SURVIVAL OF FIVE YEARS OR MORE				
			TOTAL	5-7 YR.	7-9 YR.	10-15 YR.	15 YR.
Total cases	75	40	46	14	7	4	1
Ulcerating	65	41	1	1	6	3	
Antral	22	17	3		1	1	1
Polypoid	19	14	5	1	3	1	
Infiltrating	16	12	4		2	1	
<i>In situ</i>				2			

centric origin, we naturally assume that other similar foci may be present in the residual proximal stomach. We must, therefore decide whether to perform a total gastrectomy in this 70-year-old woman with the attendant risk of this operation or to watch her constantly by fluoroscopic and gastroscopic surveillance during the remainder of her life.

*Presence or Absence of Metastases in Regio al Lymph Node.*—The absence of metastatic cancer in the lymph nodes removed with the resected stomach has always been heralded as an important factor of good prognosis in the evaluation of end results, but the total number of patients surviving without recurrence for five years after resection is so small that percentage figures offer information of only relative value. Of one patient who reached the period of definitive cure, 60 per cent did not have metastases in the perigastric lymph nodes. The surprising fact is that in the remainder of our long-term survivors, that is, 30.8 per cent of the cured cases, cancer was demonstrably present in the excised lymph nodes (Table VI). It is a truism that cancer of the stomach is not inoperable when it has passed beyond the confines of the stomach to the perigastric lymph nodes, yet this fact is often not appreciated by surgeons who refuse to perform gastrectomy because of apparently gross metastatic cancer in lymph nodes adjacent to the primary tumor. In the first place even expert pathologists frequently are in error concerning the gross appearance of cancer in lymph nodes, and in the second place such lesions if widely resected may be permanently eradicated.

The relative prognosis of patients who have undergone gastrectomy for cancer with and without metastases to regional lymph nodes may also be expressed in the following manner: (a) those without metastases to lymph nodes—42.8 per cent five-year survival, (b) those with proved metastases to lymph nodes—24.3 per cent five-year survival.

1 Pay strict attention to the digestive complaints of all patients over 40 years of age so as to establish early diagnosis

— Increase the resectability rate so that an even higher proportion of gastric tumors is resected

3. Resect all gastric cancers technically removable even if (a) the tumor is attached to an adjacent organ (spleen, colon, liver pancreas) (b) apparent metastatic cancer is seen and felt in perigastric lymph nodes (c) the entire stomach must be sacrificed or (d) the cancer involves the abdominal esophagus

4 Decrease the postoperative mortality by improvement in operative technique and close pre and postoperative supervision, so that more patients survive the operation and may hope for a curative end result

#### SUMMARY

1 In the first quarter century of effort at the Memorial Hospital for Cancer and Allied Diseases, the curability of gastric cancer was only 3 to 4 per cent of all patients with this disease. However the resectability rate in these early years was only 10 per cent which would indicate that about one third of all patients undergoing gastrectomy were cured

2 The resectability rate for gastric cancer has shown progressive improvement for each succeeding period, for example the percentage resected among all patients with gastric cancer has been 1916 to 1930 9 per cent 1931 to 1936 77 per cent 1937 to 1941 96.2 per cent 1942 to 1946 89.8 per cent. Of all patients subjected to laparotomy between 1942 and 1946 48.1 per cent had successful gastrectomy for cancer and 89 per cent of all patients with gastric cancer underwent some type of operative procedure designed for cure or palliation.

3 Of seventy-five patients surviving gastrectomy for cancer twenty-six, or 34.7 per cent lived five years without recurrence

4 The operative mortality for subtotal gastrectomy has decreased with each succeeding surgical period for example 1916 to 1930 69.6 per cent 1931 to 1936, 33.3 per cent 1937 to 1941 15 per cent 1942 to 1946 9.8 per cent

5 More than eighty patients in the last quinquennial period have had either total gastrectomy or transthoracic esophagectomy for gastric cancer (Memorial Hospital series)

6 The preoperative duration of symptoms apparently has no influence on the curability of those patients who have had gastrectomy for cancer

7 The gross pathologic type of cancer does have a bearing on the prognosis following gastric resection, for example the percentage of five year cures among the following types carcinoma in situ 100 per cent ulcerocancer 73.9 per cent polypoid cancer 96.3 per cent infiltrating cancer 22.7 per cent annular cancer 22.7 per cent

8 The presence of metastatic cancer in the perigastric lymph nodes of resected gastric cancers does influence the end result of treatment for example those patients without nodal metastases had 48.8 per cent five-year survival without recurrence and those patients with proved metastases to nodes had 24.9 per cent definite five year cures



TABLE VIII. FIVE YEAR SURVIVAL FOLLOWING RESECTION FOR GASTRIC CANCER IN RELATION TO THE HISTOLOGICAL GRADE OF TUMOR AND METASTASIS TO REGIONAL LYMPH NODES FROM 1910 THROUGH 1941

LENGTH OF SURVIVAL	FIVE YEAR SURVIVALS	HISTOLOGICAL GRADE OF TUMOR				METASTASIS TO REGIONAL LYMPH NODES	
		GRADE I	GRADE II	GRADE III	GRADE IV	WITH	WITHOUT
Total	46	5	10	9	2	8	14
5 to 7 yr	14	3	5	4	2	3	11
7 to 10 yr	7			3		3	4
10 to 15 yr	4		3	1			3
15 yrs.	1			1			1

\*Two patients have died—one of recurrent disease and one of heart disease.  
†One patient died of heart disease 10 years postoperatively.

good chance for permanent cure and, furthermore, that patients with the anaplastic Grade IV gastric cancers are not absolutely hopeless (Table VII)

*The Prognostic Significance of Gelatinous Features in Gastric Cancer.*—Billroth's first successful gastrectomy on the historic patient, Theresa Heller was for a gelatinous cancer but the patient died four and one-half months later the post mortem report emphasizing a gelatinous metamorphosis of the peritoneum. One would ordinarily think of such gelatinous features as a degenerative phenomenon and tend to attribute no significance to this occurrence but experience has shown that few patients with this type of gastric cancer are cured. The mucinous material containing groups of cancer cells early permeates the subserosal lymphatics, and diffuse peritoneal carcinosis with ascites is usually the result. In our group of nine patients who had gastrectomy for such gelatinous or mucocarcinomas, only two lived without recurrence for five years (22 per cent) although seven of these nine resected specimens revealed no evidence of metastases in perigastric lymph nodes (Table VII)

*The Prognostic Significance of Serosal Penetration by Gastric Cancer.*—We have been told that serosal penetration by gastric cancer either resulting in perforation into the abdominal cavity or fixation to an adjacent organ, such as the pancreas, liver, spleen or transverse colon, constitutes a menace as far as the prospect of cure is concerned. However it has been our experience after spending tedious hours removing such gastric cancers, even with parts of neighboring viscera, that many of these patients surprised us by living for many years. Of sixteen patients who had this complication and whose gastric cancers were still operable eight are living and well five years later (50 per cent) and one of these patients may be lauded as a sixteen year cure. In six of these eight long term survivors of gastrectomy no metastatic cancer was present in lymph nodes removed with the gastric tumor. Let us urge the surgeon, therefore to attempt the removal of these gastric cancers which are adherent to liver, pancreas, spleen, and transverse colon as it is our belief and contention that a high incidence of five year cures may be obtained, even if metastases occur in the perigastric lymph nodes.

#### CONCLUSIONS

Until the fundamental nature of gastric cancer is understood, it is difficult to escape the following conclusions:

## POSTCHOLECYSTECTOMY SYMPTOMS DUE TO CYSTIC DUCT REMNANT

CHARLES BRUCE MORTON, II, M.D. CHARLOTTESVILLE, VA.

(From the University of Virginia)

SYMPTOMS referable to the biliary tract following extirpation of the gall bladder have been designated by such names as postcholecystectomy syndrome, biliary dyskinesia, and biliary dyskinesia. In some cases a definite organic cause for the symptom has been discovered, while in others no demonstrable cause has been found. Among the more tangible causes are stone in the extrahepatic ducts, stricture or annulation of the extrahepatic ducts, cholangitis, hepatitis, pancreatitis, errors in diagnosis, ill-advised operation, neurogenic factors, and others.<sup>1-5</sup> The problems of diagnosis and differential diagnosis may be extremely difficult. Although a remnant of the cystic duct left at the time of cholecystectomy has been recognized as a cause of biliary tract symptoms, it has received relatively scant attention.

Seven personal cases in which operation revealed a cystic duct remnant to be apparently the sole cause of postcholecystectomy symptoms and in which removal of the remnant relieved the symptoms completely prompted this communication. In addition to the seven cases referred to, two more instances of cystic duct remnant have been encountered but because one was complicated by a stone in the common bile duct and the other by a stricture of the common bile duct, the latter presumably secondary to the cystic duct remnant they will not be included in the series. Both patients however had excellent results following operation.

Of the seven patients in this report two were men, five were women (Table I). Their ages varied between 28 and 73 years. In all instances the cholecystectomy had been performed elsewhere and as far as could be determined from their histories the diagnosis of gall bladder disease and the indications for surgical treatment had been adequate. The gall bladder in these patients had been removed from nine months to eighteen years before they had sought surgical relief from postcholecystectomy symptoms. In all cases there had been both pain and jaundice both of which in some instances had been marked in degree. Symptoms had appeared first after cholecystectomy from at once to fifteen years.

The diagnosis in each case prior to operation of a postcholecystectomy syndrome was a suspected stone in the common duct though in the last three because of experience in the previous cases a duct remnant had been recognized as an additional possibility. The operative procedure in each case in addition to general exploration and partial inspection of the liver, duodenum, and pancreas was directed at accurate exposure of the extrahepatic duct and careful exploration of them by probing and irrigation. In each case the cystic duct

9 The histologic grade of the resected gastric cancer has a most decided bearing on the number of five-year definitive cures, for example, Grade I, 100 per cent Grade II 41.7 per cent Grade III 30 per cent Grade IV 16 per cent.

10 The so-called gelatinous or mucocarcinoma of the stomach is nearly always attended by a bad prognosis. Only 22 per cent of this small group of patients achieved the five-year period of definitive cure although seven of these nine patients did not have metastatic involvement of perigastric lymph nodes.

11 Local serosal penetration resulting in fixation to adjacent organs whose removal is compatible with life may be a favorable rather than an unfavorable complication perhaps because of the more radical operation that must necessarily be done. In our own series of sixteen patients who had these radical operations, eight were living and well five years later a curability of 50 per cent.

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Seven personal cases in which operation revealed a cystic duct remnant to be apparently the sole cause of postcholecystectomy symptoms and in which removal of the remnant relieved the symptoms completely prompted this communication. In addition to the seven cases referred to two more instances of cystic duct remnant have been encountered but because one was complicated by a stone in the common bile duct and the other by a stricture of the common bile duct, the latter presumably secondary to the cystic duct remnant they will not be included in the series. Both patients, however, had excellent results following operation.

Of the seven patients of this post two were men and five women (Table I). Their ages varied between 28 and 73 years. In all instances the cholecystectomy had been performed elsewhere and as far as could be determined from their histories the diagnosis of gall bladder disease and the indications for surgical treatment had been adequate. The gall bladder in these patients had been removed from nine months to eighteen years before they had sought surgical relief from postcholecystectomy symptoms. In all cases there had been both pain and jaundice both of which in some instances had been marked in degree. Symptoms had appeared first after cholecystectomy from one to fifteen years.

The diagnosis in each case prior to operation of postcholecystectomy symptoms was a suspected stone in the common bile duct though in the last three because of experience in the previous cases, a cystic duct remnant had been recorded as an additional possibility. The operative procedure in each case, in addition to general exploration and particular inspection of the liver duodenum and pancreas was directed at accurate exposure of the extrahepatic duct and careful exploration of them by probing and irrigation. In each case the cystic duct

TABLE I

AGE IN YEARS	PREVIOUS SURGERY	SEX	AGE ( )	DATE OF CYSTO- TOMY RE- WHOLE	INTERVAL BEFORE TOMY TUMOR RECEIVED	DATE OF REMOVAL OF CYSTIC DUCT REMARKS	FOUR OF CYSTIC DUCT REMARKS (CM)	FOLLOW UP REMARKS (1947)	FOLLOW UP INTER- VAL (YE)
1	A. T. L. (14711)	M	64	1922	15 y	Jul 31 1939	2.5	Excellent	7
	L. T. (171705)	F	20	1932	8 y	Sept. 2, 1941	3.4	Excellent	8+
2	H. L. B. (190915)	F	73	1930	5 yr	July 19 1944	1	Dull	2
4	J. H. C. (311152)	F	55	1943	8 yr	March 1, 1943	2.5	Excellent	2
5	M. G. W. (219070)	M	36	1943	At once	Xer 21, 1943	4.0	Excellent	1
6	G. E. M. (220173)	F	63	1943	At once	Nov 14 1943	3.4	Excellent	1
7	J. M. C. (223321)	F	43	1928	6 y 1 y f	Feb 2, 1944	1.5	Excellent	1

Until cholecystectomy in 1924

† additional later 1 after cholecystectomy

remnant was ligated at its entrance into the common duct and excised. A T tube was left in the common duct for temporary drainage and decompression. At various intervals of time the tube was tied off and finally removed. Because of equivocal and sometimes misleading results postoperative cholangiograms have not been used routinely by me and were not employed in any of this series.

The result in each of the seven patients was excellent after operation. All patients have been heard from recently either by personal interview or letter and none have had recurrent symptoms. The follow-up intervals are between one and one-half and seven and one-half years.

#### CASE REPORTS

CASE 1.—A. T. L., male, aged 64 years, entered the University of Virginia Hospital July 3, 1939. He complained of recurring acute attacks of abdominal pain and jaundice during period of twenty six months. The attacks were at first spaced weeks or months apart, but during the preceding month had occurred every few days. Pain had been localized in the right upper abdomen, had radiated to the right scapular region, had been severe, had required opiates for relief, and had been followed by emotional nervousness, jaundice, highly colored urine, and in colored stool had been accompanying symptoms. He had lost sixteen pounds in three or four months. He stated that the attacks had been similar to those preceding an operation he underwent elsewhere in 1922 for the removal of gall bladder containing numerous stones. Removal of stones from the common bile duct. Gall bladder symptoms, however, had appeared for the first time as early as 1911.

Postoperative physical findings were moderate anemia and a healed scar in the right upper abdomen with moderate tenderness in the region without muscle spasm or mass. Pertinent laboratory studies included: serum index of 51 which in eighteen days fell to 40; bile in the urine and both haptoglobin and urobilinogen in the stool.

The diagnosis, stones in the common bile duct, proved obvious and operation is advised. The operation was performed July 1, 1939. Under spinal anesthesia with patient under the abdomen placed through the skin of the previous incision. Afterward of leaving the former operation area not troublesome and general exploration was negative except related to the common bile duct. It was moderately dilated but otherwise normal.

except at its proximal part here diverticular like pocket discovered. This proved to be cystic duct remnant dilated to more than 1 cm in diameter. Just distal to it along the common bile duct there was lymph gland more than 1 cm. in diameter. The common duct was incised just distal to the cystic duct remnant and careful exploration with probing and irrigation as negative for stone or other abnormality. Visualization of the papilla of Vater through an incision into the duodenum revealed nothing. The cystic duct remnant was excised and its communication with the common duct ligated. The adjacent lymph gland was removed and T tube left in the common duct. Pathologically the cystic duct remnant showed chronic inflammation and the lymph gland chronic lymphadenitis.

Convalescence was uneventful and the patient was discharged from the hospital on the sixteenth postoperative day with the T tube still in place but tied off since the ninth day following its introduction. The tube was removed nine weeks after operation. A follow up letter May 23, 1917 reported excellent health and no biliary tract symptoms from the time of removal of the cystic duct remnant, nearly eight years previous.

CASE 1.—L. T. woman aged 39 years, entered the University of Virginia Hospital Aug 29 1911. She complained of three attacks in eight months of acute abdominal pain. All attacks had been similar acute colicky pain in the epigastrium with some nausea and vomiting. There had been no radiation of the pain but its severity had necessitated the administration of opiates. Clay colored stools and jaundice had been noticed. Nine years previously she had been operated upon elsewhere for gall bladder trouble but she did not know what the operative findings or procedures.

Physical examination revealed nothing more than moderate jaundice and an enlarged area in the right upper abdomen with tenderness and muscle spasm in the region. There was slight temperature elevation, and an asterix index of 31 was the only important laboratory finding. Because of uncertainty as to previous removal of the gall bladder the preoperative diagnosis thought to be stone in the common bile duct with or without cholangitis.

Operation as performed Sept 3, 1911. Spinal anesthesia and an incision through the old scar were employed. Many adhesions were encountered and, therefore, only the upper abdomen was explored. The gall bladder had been removed and no abnormality was found except for large bile duct about 1.5 cm. in diameter and large cystic duct remnant dilated to more than 1 cm. in diameter. Careful exploration of the common duct by probing and irrigation through an incision into the duct just distal to the cystic duct remnant failed to reveal a stone or other abnormality. Graduated dilators up to the 8 mm. size passed readily into the duodenum. The cystic duct remnant was excised after ligating its attachment to the common duct and T tube was left in the common duct. Pathologically the cystic duct remnant showed chronic inflammation.

Convalescence was uneventful and the T tube tied off ten days after operation and removed fourteen days after operation. The patient left the hospital on the fifteenth postoperative day. A follow up interview and examination April 9 1917 showed freedom from symptoms referable to the biliary tract since removal of the cystic duct remnant more than 5 and one-half years previous.

CASE 2.—H. L. B. woman aged 73 years entered the University of Virginia Hospital Jul 10, 1914. She complained of frequent pain in the epigastrium and back of three months duration and jaundice of three week duration. The pain had been more on the right of the midline and radiated to the back in the scapular region, and usually had not been very severe. She had had similar pain without jaundice for one year preceding an operation somewhere a year before. The gall bladder had been removed and found to contain two small stones.

Physical examination revealed no evidence of the operation, moderate jaundice and what appeared to be slight enlargement of the liver. Laboratory studies showed bile in the urine, no bile in the stools and an asterix index of 146. Obstructive jaundice due to probable stone in the common bile duct was diagnosed. A operation followed.

Operation was performed July 19, 1944 under ether anesthesia. The scar of the previous incision through the upper part of the rectus muscle on the right side was excised and the abdominal cavity explored after separation of numerous adhesions. Nothing abnormal was found except the common bile duct and its branches. Between 1 and 2 cm. of the cystic duct remained with evidence of scarring and thickening of it and of the adjacent common duct. The common duct incised just proximal to this point and thoroughly explored by probing and irrigating. No stone was found but there was some narrowing and thickening of the common duct where the cystic duct remnant lay in contact with it. Dilators were employed and passed readily into the duodenum. The cystic duct remnant was excised free of its attachment to the common duct had been ligated and T tube was left in the common duct. Pathologically the cystic duct remnant showed fibrous scarring.

Convalescence from the operation was uneventful and the T tube was tied off twenty-four days after operation and the patient was discharged from the hospital Aug. 27, 1944. The reterus index twenty seven days after operation was 6. The T tube remained Oct. 14, 1944 and at that time the reterus index was 8.

Follow-up interview and examination Sept. 1946, indicated entire freedom from biliary tract symptoms and no signs of abnormality in more than ten years since removal of the cystic duct remnant. May 24, 1947, she reported continued freedom from symptoms, nearly three years after removal of the cystic duct remnant.

Case 4—J. H. C. female aged 34 years, entered the University of Virginia Hospital March 11, 1943. She complained of paroxysmal attacks of severe pain in the upper abdomen on the right side since the age of 14 years, such pains in all. The attacks had been later ruptured for periods of only six weeks following cholecystectomy elsewhere ten years before. She had been told there was stones in the gall bladder. Pains had been very severe had required hypodermics for relief and had been more frequent with nausea, vomiting, jaundice and clay stool. Recently the attacks had been very frequent.

Examination negative except for slight jaundice, the upper abdominal area on the right side and moderate tenderness in the region. Laboratory studies were normal except for an reterus index of 14 and prothrombin time of 15 seconds with control of 12 seconds. Operation was advised on the belief that there was probably stones in the common bile duct.

Operation was performed March 21, 1943. Spinal anesthesia was employed and the abdomen explored through an incision extending like the previous one. No abnormality was found except in relation to the common bile duct. The duct was slightly dilated and was rigid within it and cut near cost there was cystic duct remnant 8 cm. in length. The remnant extended partly round the common duct and ended its distal aspect. The common duct incised and explored, probing and irrigating it. No stone structure or other abnormality was discovered. Graduated dilators including one 7 mm. in diameter passed readily into the duodenum. The cystic duct remnant was ligated freely with the common duct and excised. The T tube was left in the common duct. Pathologically the cystic duct remnant showed marked periductal fibrosis.

Convalescence was uneventful. The T tube was tied off eight days after operation and removed two days later. The patient was discharged from the hospital April 4, 1943, thirteen days after operation.

Follow-up by letter Sept. 1, 1946, nearly one and one-half years later indicated that the patient had had no trouble or return of any pain as the result of the operation for removal of the cystic duct remnant. Another follow-up report June 7, 1947, indicated freedom from biliary tract symptoms more than two years after removal of the remnant.

Case 2—M. Q. W. male aged 36 years entered the University of Virginia Hospital Nov. 19, 1943. He complained of attacks of severe pain in the epigastrium during the previous one and one-half months and attacks of milder pain in the epigastrium and right upper abdomen since June 12, period of nearly one and one-half years. In June 1943, he underwent operation elsewhere for removal of the gall bladder after suffering for nearly months

with periodic attacks of typical acute gall bladder colic without jaundice. The gall bladder was said to contain three stones. Immediately following the operation not a week passed as he did not suffer from marked indigestion or bloating or gas pains. Jaundice had been noticed occasionally. Attacks of very severe pain in the epigastrium with radiation to the scapular regions of the back similar to those suffered prior to cholecystectomy had occurred during the preceding one and one-half months. Clay-colored stool and jaundice had been noted by him. Some relief had been afforded only by hypodermics.

Examination was negative except for well-healed surgical scar in the right upper abdomen with moderate tenderness and muscle spasm in the region and light tenderness. Laboratory studies were negative except for serum indices varying between 2 and 17. Because of experience with the preceding case in this series it was thought that the patient had either stone in the common bile duct or cystic duct remnant and operation was advised.

Operation performed Nov. 1, 1943, under spinal anesthesia. This incision was made through the previous scar. General abdominal exploration was negative except for slight enlargement of the common bile duct and cystic duct remnant 4 cm. length lying long the right side of the common bile duct. The remnant dissected free about 1 inch with the common duct and removed. The common duct measured distal to this point not explored by probing and irrigation and the passage of graduated dilators into the duodenum up to the 7 mm. size. No stone or other abnormality as found. A T tube was left in the common duct. Pathologically the cystic duct remnant showed no inflammation.

Convalescence unremarkable. The T tube was tied off five days after operation and removed three days later. The patient discharged from the hospital eleven days following operation. He reported by letter June 13, 1944, one and one-half years after removal of the cystic duct remnant that he had been entirely relieved. He had only slight indigestion after returning to his old eating habits.

CASE 6—G. E. M., woman, aged 63 years, entered the University Hospital Dec. 4, 1943. She complained of attacks of pain in the upper abdomen toward the right during eleven months. She had commenced the gall bladder symptoms in 1942 and under went operation elsewhere March 22, 1943. The gall bladder which contained many calculi, was removed. For some weeks after operation she continued to have recurring attacks of sharp cramping pain in the epigastrium with radiation to the right shoulder and vomiting. Hypertensions are necessary to relieve pain and there is residual nervousness. No jaundice and no clay-colored stool ever in last two years. Dark clay attacks. The attacks however ceased for almost six months but reappeared and became more severe and frequent during the five months preceding hospitalization.

Examination was negative except for some tenderness in the region of the surgical scar in the right upper abdomen. All other examinations negative. Laboratory studies were normal except for serum indices ranging between 10 and 18. These the common duct or cystic duct remnant was suspected and an exploratory operation was advised.

Operation was performed Dec. 14, 1943, under spinal anesthesia. Exploration of the abdomen was made through the scar in the right upper abdomen. There were no many dense adhesions that hid the upper abdomen. Explored. Nothing abnormal as found except for dilatation of the common duct to diameter of proximal of 1.3 cm. and cystic duct remnant more than 3 cm. in length. The common duct was opened and explored by probing and irrigation. About diverging stone structure or an other abnormality. Graduated dilators including one 7 mm. in size passed readily in the duodenum. The cystic duct remnant was ligated at its entrance at the common duct and removed. A T tube was left in the common duct. Pathologically the cystic duct remnant showed chronic inflammation and little pus-like material within lumen of wall.

Convalescence unremarkable. After operation and four days the T tube was tied off. It was removed five days later. The patient discharged from the hospital fourteen days after operation. He was up through Dec. 16, 1944, remained free from biliary tract symptoms for three years after removal of the cystic duct remnant.



**CASE 7—J M O** woman, aged 45 years, entered the University of Virginia Hospital Jan. 31, 1946. She complained of attacks of pain in the right upper abdomen, three during the preceding six weeks. Pain had been severe with radiation to the right scapular region and with nausea and vomiting. Jaundice had occurred, hypodermics had been necessary for pain control, and there had been residual soreness. She referred to two previous operations performed elsewhere, one in 1928 for removal of extra-hepatic gall bladder and one in 1931 for removal of stones from the common bile duct.

**Examination**—as negative except for light tenderness in the region of surgical scar in the right upper abdominal wall. There was no jaundice and laboratory studies were normal. Stone in the common duct or cystic duct remnant was suspected and operation advised.

**Operation**—as performed Feb. 7, 1946. Spinal anesthesia as employed and the incision was made through the scar of the previous right upper abdominal incision. No abnormality was found except for slight enlargement of the common bile duct which was little more than 1 cm in diameter and cystic duct remnant 1.5 cm in length. The common duct as incised and explored by probing and irrigation but no stone or other abnormality was found. Graduated dilators of 6 mm in diameter passed readily into the duodenum. The cystic duct remnant was ligated flush with the common duct and excised. A T tube was left in the common duct. Pathologically the cystic duct remnant showed chronic inflammation.

Convalescence was uneventful and the T tube was tied off four days after operation and five days later as removed. The patient was discharged from the hospital on the thirteenth postoperative day. Follow up interviews and examination Oct. 8, 1946, eight months after operation, revealed complete freedom from biliary tract symptoms and signs. Re-examination Sept. 22, 1947 revealed no trouble more than one and one-half years after removal of the remnant.

#### COMMENT

Seven instances of cystic duct remnant presumably solely responsible for symptoms in patients previously subjected to cholecystectomy elsewhere have been described. In two others, not reported, a cystic duct remnant was probably related to postcholecystectomy symptoms. The cases occurred in a period of only seven years and in the experience of a single surgeon. Although these patients sought surgical treatment because of the severity of the symptoms, it is probable that others with similar trouble did not seek operation because of less severe symptoms. It seems likely therefore that a cystic duct remnant may be a frequent source of postcholecystectomy symptoms.

In reporting a uniformly excellent result in all of the cases it is realized that the follow-up interval is possibly too short to insure permanent freedom from biliary tract symptoms. The symptoms attributed to the cystic duct remnant did not appear recognizable degree until from fifteen years to immediately following cholecystectomy. The follow-up periods vary from nearly eight years to over one and one-half years (Table I).

Surgical literature bounds in technical descriptions of cholecystectomy but in referring to division of the cystic duct in the case of cholecystectomy the emphasis is on avoidance of common duct injury with little except in very recent years indicating that long scope of the cystic duct may cause trouble. In extreme example is found in one case report consulted. In the description of cholecystectomy the statement occurs in referring to division of the cystic

duct— It should not be clamped until it has been clearly isolated close to the gall bladder.

Because of the serious consequences of injury to the common duct every precaution should be observed to protect it, but this attitude should not cause one to leave a cystic duct remnant which, as shown by the cases of the 1st post and others, may cause symptoms and necessitate another operation with its attendant magnified risks and dangers.

Anatomically the cystic duct has been said to average 1 cm in length and to follow a downward course parallel to the hepatic duct on its right and anterior surface for a variable distance before it actually empties into the latter to form the common bile duct.<sup>12</sup> Actually variations of the cystic duct are extreme both as to length and as to course. Graham and associates<sup>13</sup> reported at length the variations in the extrahepatic ducts and adjacent blood vessels. Four pages of text and thirty diagrams illustrate various abnormalities in the arteries and the extrahepatic bile duct met with in gall bladder surgery. These and other considerations fortifiably support the statement of Hsicken and co-workers,<sup>14</sup> "Experience dictates that no physician should elect to operate on the gall bladder unless his training and familiarity with the biliary system will permit him to explore the large bile duct and correct complicated intraductal problems."

I have been impressed by the frequency with which the cystic duct is so intimately associated with the common duct that they seem to be encompassed by a common adventitial covering and also by the fact that the cystic duct not uncommonly follows a spiral course along much of the circumference of the common duct and enters it dorsally rather than ventrally or laterally as in most instances. Graham and associates called attention to these as well as many other variations.

As to the mechanism by which a cystic duct remnant may cause symptoms, various authors differ. Bevel<sup>15</sup> thought the dilatation of the remnant and the formation of a gall bladder-like diverticulum to be important. Ivy and Sandblom<sup>16</sup> and others believed the influence of the choledochoduodenal mechanism of reciprocal innervation to be important. Womack and Fowler<sup>17</sup> referred to the neuroma-like scarring associated with the remnant and McDonald<sup>18</sup> stressed the focus of infection resident in the remnant.

It seems possible that the close anatomic juxtaposition of the cystic and common duct may offer the simplest explanation of the mechanism by which a cystic duct remnant left in the course of cholecystectomy causes clinical manifestations. The equally diseased duct remains after the diseased gall bladder has been removed. The valves of Hester and the tangential implantation of the cystic in the common duct promote stasis and harbor or invite infection. Periodic exacerbations of the infection with edema and possibly some resultant extraneous obstruction of the adjacent common duct may with or without an accompanying widespread cholangitis and hepatitis, explain the pain and jaundice which are the characteristic clinical manifestations attributed to a cystic duct remnant.



## VASCULAR THROMBOSIS IN ACUTE APPENDICITIS

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THE histologic examination of appendices removed in cases of acute appendicitis, thrombosis of small vessels occasionally has been noted. This study was undertaken to determine the origin and frequency of occurrence of thrombosis and, if possible, their relationship to the course of the disease.

Modern text on surgery and pathology make little or no mention of the occurrence of thrombosis in acute appendicitis. While the literature on acute appendicitis is voluminous and includes several thousand articles, the vascular factor in this disease has received comparatively little attention.

Aschoff's views on the pathogenesis of acute appendicitis are the basis of present-day teaching. Aschoff's monograph makes little reference to vascular lesions or circulatory disturbances. These were regarded as purely secondary to acute appendicitis.

Van Cott in the chapter on pathology in Fowler's monograph on appendicitis, described paravascularitis, perivascularitis, endovascularitis and thrombosis of the mesenteric vessels and included that torsion of the mesentery resulted in vascular and nutritional changes that caused interference with the nutrition of the appendiceal tissues and thus opened the way to infection.

De Kleek included on the importance of circulatory disturbances as an etiologic factor in appendicitis. He outlined the belief that such disturbances might follow kinking or torsion of the appendix or its mesentery.

Meissel found frequent vascular lesions of the meso-appendix and stated the belief that these were of primary significance in appendicitis. Von Brunn found thrombotic and irritating vascular lesions in all but one of twenty cases of appendicitis. He disagreed with Meissel, however, as to their significance and stated that he thought them secondary rather than primary to the infection.

Graham suggested that the reason for the frequency of occurrence and the occasionally rapid fatal course of appendicitis is interference with the circulation of the appendix, which is of the terminal or peripheral type and is peculiarly prone to mechanical blockage by angulation, kinking, or torsion. He added that terminal constriction may readily produce stasis of the blood stream.

Modern thought concerning the cause of acute appendicitis is in accord with the teachings of Aschoff; however, as a result of the work of Wangensteen and his associates, the importance of appendiceal obstruction in the pathogenesis of acute appendicitis now is recognized.

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Vascular thrombosis was noted by John Hunter<sup>2</sup> in veins passing through inflamed tissues. In a paper read in 1784 he described the walls of veins as being adherent and stated that the adhesions arose from the extravasation of coagulable lymph thrown out by the exhalants on the internal surface of the vein.

Bell<sup>3</sup> has mentioned the importance of infection in the production of thrombosis. The suppurative process may extend to the vessel and cause injury to the vascular endothelium. Modern textbooks of pathology agree that thrombosis starts as the deposition of blood platelets on a roughened area of intima. Endothelial damage, slowing of the blood stream, and changes in the composition of the blood are cited as the causes of thrombosis.

#### MATERIAL AND METHOD OF STUDY

Histologic studies were made on 100 appendices removed in consecutive cases of acute appendicitis. The appendix in each case had been fixed in formalin immediately after removal. The organ was cut transversely and examined grossly for areas of necrosis or perforation. Multiple sections were cut in the plane throughout the entire length, about three sections being made to the centimeter. Blocks were then cut from any part which presented gross evidence of necrosis or from representative part of the appendix. Three to five blocks were made from each appendix and the blocks were sectioned and stained with hematoxylin and eosin for microscopic examination.

The criterion for thrombosis in the specimens examined was the presence of fibrin and fibrocytes within a vessel whose walls could definitely be identified. This eliminated the identification of any of the various types of capillary thrombosis differentiated by Aschoff<sup>4</sup> and others.<sup>5-7</sup> However this strict standard was necessary as positive identification of thrombosis in small vessels and capillaries is impossible in specimens in acute appendicitis in which exudation of protein material and the presence of cell and debris within the lumen spaces of the organ are evident.

The clinical history then was reviewed in each case and the age, sex, duration of symptoms, and the leukocyte count were noted as well as the pathogenetic course of the patient.

#### RESULTS OF INVESTIGATION

Evidence of thrombosis was found in one or more vessels in twenty six of the 100 appendices examined. In nine of these twenty-six specimens the thrombosis occurred only in arteries. In twelve specimens the thrombosis occurred only in veins and in five specimens it occurred both in arteries and veins. At sites of thrombosis there did not appear to be an more marked inflammatory reaction in the tissues immediately surrounding the vessel than in the adjacent areas.

Most of the thrombi were at an early stage of development and all occurred in small vessels from 100 to 400 micron in diameter (Figs 1 and 2, a and b). Recanalization was found in one case. This occurred in girl 11 years old who gave a history of acute appendicitis of twenty hours duration.

In six appendices only one thrombosed vessel was found in each. The greatest number found in any one specimen was ten and the average number found per organ of the twenty-six which contained thrombosed vessels was 3.3.



Fig. 1—Early thrombosis of major cutaneous longitudinal section (h. matrix, low magnification, X70).

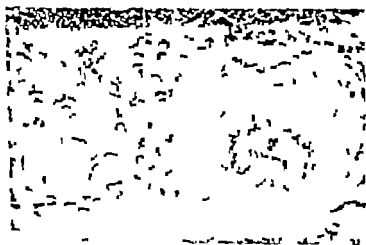


Fig. 2—Thrombosis of a vessel in the submucosa (h. matrix, low magnification, X70).

Of the eighty-seven thrombosed vessels seen sixty-four were in the submucosa, twenty-two in the subserosa and none in the muscularis. The majority of thrombosed vessels were seen in the distal third of the appendix.

Gangrenous rupture of the appendix and fecaliths were found more frequently in the group of specimens with thrombosed vessels than in the group of specimens without thrombosis (Table I).

TABLE I. I. COMPARISON OF GANGRENE, RUPTURE OF THE APPENDIX, AND FATALITY IN APPENDICITIS WITH AND WITHOUT THROMBOSIS OF VEINS

	WITH THROMBOSIS (26 CASES)		WITHOUT THROMBOSIS (74 CASES)	
	CASES	PER CENT	CASES	PER CENT
Gangrene	18	69.2	20	27.0
Rupture	5	19.2	4	5.4
Fatality	13	50.0	15	20.3

Data regarding the duration of symptoms, leucocyte count, and age of patients who had appendicitis with and without thrombosed vessels are given in Table II. There were two children 4 years of age who had thrombosis of the appendiceal vessels. One child was 8 years old and three were 9 years old. The oldest person who had thrombosis of the appendiceal vessels was 64 years old.

Fifty-four per cent of the patients in the group with thrombosis and 46 per cent in the group without thrombosis were males.

TABLE II. II. COMPARISON OF DURATION OF SYMPTOMS, LEUCOCYTE COUNT, AND AGE OF PATIENTS WITH AND WITHOUT APPENDICITIS WITH AND WITHOUT THROMBOSIS OF VEINS

	WITH THROMBOSIS (26 CASES)	WITHOUT THROMBOSIS (74 CASES)
Average duration of symptoms (hours)	16	31
Average leucocyte count	19,300	14,200
Average age (years)	2.0	27.2

One abscess in the operative wound developed postoperatively in the group with thrombosed vessel and three abscesses in the wound and one in the pelvis occurred in the group in which thrombosis was not found.

#### COMMENT

It is apparent that the evidence of thrombosis found in the specimens examined in this study was secondary to acute appendicitis. This can be concluded from several findings: (1) wherever evidence of thrombosis was found it was minimal and was present in an extremely small fraction of the total number of vessels in each section; (2) the thrombosed vessels were very small; (3) the surrounding inflammatory reaction was no more marked in the immediate vicinity of the thrombosed vessel than in the adjacent area.

The element of time also supports the view that the thrombi found in this study were secondary to acute appendicitis. The duration of symptoms averaged three hours longer in cases in which thrombi were present than in cases in which thrombi were absent.

The majority of thrombosed vessels were found in the submucosa. Although the circulation is of the terminal or peripheral type, the vessels anastomose freely. Koster and Weintraub, from their experimental studies, commented on the richness and responsiveness of anastomosis and showed that the blood supply is in two layers of which the richer is the deeper or submucosal layer. The fact that the majority of the thrombosed vessels were in the freely anastomosing submucosal layer probably contradicts the notion that the thrombosis was caused by stagnation of the flow of blood. Rather the thrombosis occurred as a result of endothelial damage and extension of the surrounding inflammation.

Thrombosis is thought to occur more frequently in older people. This apparently is not true of thrombosis which occurs in the vessels of acutely inflamed

appendices thus, in this series the average age in the cases in which thrombosis occurred was nearly the same as that in cases in which thrombosis did not occur (Table II). In two cases in which thrombosed vessels were found the patients were 4 years of age.

The higher average leucocyte count in the group with thrombosed vessels as compared with that in the group without thrombosis can be explained in part at least, by the longer duration of symptoms before removal of the diseased appendix in the former group (Table II). The higher incidence of gangrene and rupture in the group with thrombosis also explain the higher leucocyte count.

It is supposed that the longer duration of the disease in the group with thrombosed vessels as compared to the group without thrombosed vessels partly explains the higher incidence of gangrene and rupture in the group with thrombosis (Table II). This supposition is supported by the fact that the average duration of symptoms in cases of gangrene or rupture in both groups of cases was forty three hours.

The incidence of fecaliths in the cases in which thrombosed vessels were found was considerably higher than that in the cases in which thrombosis was not found (Table I). This should not be interpreted to mean that the presence of fecaliths directly influences the production of thrombosis. The relationship is undoubtedly indirect. Tennison and Dixon<sup>22</sup> have shown from a study of 1974 cases of appendicitis that the incidence of gangrene in appendicitis is higher in the presence of fecaliths. The presence of thrombosed vessel in acute appendicitis appears to be dependent to an extent on the duration of symptoms and the severity of the disease.

The significance of thrombosed vessel in acute appendicitis cannot be determined with definitiveness. Gangrene of any tissue is due directly to interference with its blood supply. The indirect cause may be infection or pressure which in turn brings about the impairment of the blood supply to the tissue. The presence of gangrene and rupture in a much higher percentage of appendices with thrombosed vessels than in those without thrombosis cannot be disregarded. It may be assumed from the higher incidence of thrombosed vessels in gangrenous than in nongangrenous appendices and from the very nature of gangrene itself that most gangrenous appendices would be found to contain thrombosed vessels if serial sections were made from such specimens.

The question of phlephlebitis as a complication of acute appendicitis arises in any consideration from thrombosis that occurs in appendicitis. Hanks<sup>23</sup> stated that in certain acutely inflamed appendices there is rapid death of the part with the formation of a protective thrombus in the venous radicles. He further stated that the thrombus may extend upward if it is not removed or related at the time of operation. In a study of 1463 cases of appendicitis he found twenty-four cases in which the complication of phlephlebitis occurred, with a death rate of 33 per cent in these twenty-four cases. Colp<sup>24</sup> recommended ligation of the ileocolic vein just before the appendix is removed if a diagnosis of phlephlebitis has been made.

In this series of cases there was no relationship between the presence of thrombosed vessels and the postoperative course of the patient.



TABLE I. INCIDENCY OF GANGRENE, RUPTURE OF THE APPENDIX, AND FATALITY IN APPENDICITIS WITH AND WITHOUT THROMBOSIS OF VESSEL

	WITH THROMBOSIS (26 CASES)		WITHOUT THROMBOSIS (74 CASES)	
	CASES	PER CENT	CASES	PER CENT
Gangrene	18	67.7	20	27.0
Rupture	8	30.2	4	5.4
Fatality	13	50.0	18	24.3

Data regarding the duration of symptoms, leucocyte count, and age of patients who had appendicitis with and without thrombosed vessels are given in Table II. There were two children 4 years of age who had thrombosis of the appendiceal vessels. One child was 8 years old and three were 9 years old. The oldest person who had thrombosis of the appendiceal vessels was 61 years old.

Fifty-four per cent of the patients in the group with thrombosis and 46 per cent in the group without thrombosis were males.

TABLE II. DATA ON DURATION OF SYMPTOMS, LEUCOCYTE COUNT, AND AGE OF PATIENTS WITH AND WITHOUT THROMBOSIS OF VESSEL

	WITH THROMBOSIS (26 CASES)		WITHOUT THROMBOSIS (74 CASES)	
	PER CENT	PER CENT	PER CENT	PER CENT
Average duration of symptoms (hours)	18	69.2	11	14.9
Average leucocyte count	14,700	56.5	11,700	15.8
Average age (years)	2.6	10.0	22.4	30.3

One abscess in the operative wound developed postoperatively in the group with thrombosed vessel and three abscesses in the wound and one in the pelvis occurred in the group in which thrombosis was not found.

## COMMENT

It is apparent that the evidence of thrombosis found in the specimens examined in this study was secondary to acute appendicitis. This can be concluded from several findings: (1) wherever evidence of thrombosis was found it was minimal and was present in an extremely small fraction of the total number of vessels in each section; (2) the thrombosed vessels were very small; (3) the surrounding inflammatory reaction was no more marked in the immediate vicinity of the thrombosed vessel than in the adjacent area.

The element of time also supports the view that the thrombi found in this study were secondary to acute appendicitis. The duration of symptoms averaged three hours longer in cases in which thrombi were present than in cases in which thrombi were absent.

The majority of thrombosed vessels were found in the submucosa. Although the circulation is of the terminal or peripheral type, the vessel anastomoses freely. Koster and Weintraub, from their experimental studies, commented on the richness and profuseness of anastomosis and showed that the blood supply is in two layers, of which the inner is the deeper submucosal layer. The fact that the majority of the thrombosed vessels were in the freely anastomosing submucous layer probably contradicts the notion that the thrombosis was caused by stagnation of the flow of blood. Rather the thrombosis occurred as a result of endothelial damage and extension of the surrounding inflammation.

Thrombosis is thought to occur more frequently in older people. This apparently is not true of thrombosis which occurs in the vessels of acutely inflamed

appendicitis thus, in this series the average age in the cases in which thrombosis occurred was nearly the same as that in cases in which thrombosis did not occur (Table II). In two cases in which thrombosed vessels were found the patients are 4 years of age.

The higher average leukocyte count in the group with thrombosed vessel as compared with that in the group without thrombosis can be explained in part, at least by the longer duration of symptoms before removal of the diseased appendix in the former group (Table II). The higher incidence of gangrene and rupture in the group with thrombosis also explains the higher leukocyte count.

It is supposed that the longer duration of the disease in the group with thrombosed vessels as compared to the group without thrombosed vessel partly explains the higher incidence of gangrene and rupture in the group with thrombosis (Table II). This supposition is supported by the fact that the average duration of symptoms in cases of gangrene or rupture in both groups of cases was forty three hours.

The incidence of fecaliths in the cases in which thrombosed vessel were found was considerably higher than that in the cases in which thrombosis was not found (Table I). This should not be interpreted to mean that the presence of fecaliths directly influences the production of thrombosis. The relationship is undoubtedly indirect. Tennison and Dixon<sup>22</sup> have shown from a study of 1244 cases of appendicitis that the incidence of gangrene in appendicitis is higher in the presence of fecaliths. The presence of thrombosed vessel in acute appendicitis appears to be dependent to an extent on the duration of symptoms and the severity of the disease.

The significance of the thrombosed vessels in acute appendicitis cannot be determined with definiteness. Gangrene of any tissue is due directly to interference with its blood supply. The indirect cause may be infection or pressure which in turn brings about the impairment of the blood supply to the tissue. The presence of gangrene and rupture in a much higher percentage of appendices with thrombosed vessel than in those without thrombosis cannot be disregarded. It may be assumed from the higher incidence of thrombosed vessels in gangrenous than in nongangrenous appendices and from the very nature of gangrene itself that most gangrenous appendices would be found to contain thrombosed vessels if serial sections were made from such specimens.

The question of phlephlebitis as a complication of acute appendicitis arises in no consideration from thrombosis that occurs in appendicitis. Hawkes<sup>23</sup> stated that in certain acutely inflamed appendices there is rapid death of the part with the formation of a pyogenic thrombus in the venous radicles. He further stated that the thrombus may extend upward if it is not removed or isolated at the time of operation. In a study of 1467 cases of appendicitis he found twenty four cases in which the complication of phlephlebitis occurred, with a death rate of 33 per cent in these twenty four cases. Culp<sup>24</sup> recommended ligation of the ileocolic vein just before the appendix is removed if a diagnosis of phlephlebitis has been made.

In this series of cases there was no relationship between the presence of thrombosed vessels and the postoperative course of the patient.

TABLE I. INCIDENCE OF GANGRENE, RUPTURE OF THE APPENDIX, AND FETALITY IN APPENDICITIS WITH AND WITHOUT THROMBOSED VESSELS

	WITH THROMBOSES (26 CASES)		WITHOUT THROMBOSES (46 CASES)	
	CASES	PER CENT	CASES	PER CENT
Gangrene	13	87.5	30	27.0
Rupture	5	19.2	4	8.4
Fetal it	12	80.0	18	39.3

Data regarding the duration of symptoms, leucocyte count and age of patients who had appendicitis with and without thrombosed vessels are given in Table II. There were two children 4 years of age who had thrombosis of the appendiceal vessels. One child was 8 years old and three were 9 years old. The oldest person who had thrombosis of the appendiceal vessels was 63 years old.

Fifty-four per cent of the patients in the group with thrombosis and 46 per cent in the group without thrombosis were males.

TABLE II. DATA ON DURATION OF SYMPTOMS, LEUCOCYTE COUNT AND AGE OF PATIENTS WITH APPENDICITIS WITH AND WITHOUT THROMBOSED VESSELS

	WITH THROMBOSES (26 CASES)	WITHOUT THROMBOSES (46 CASES)
Average duration of symptoms (hours)	32	33
Average leucocyte count	19,500	14,900
Average age (years)	22.0	25.2

One abscess in the operative wound developed postoperatively in the group with thrombosed vessels and three abscesses in the wound and one in the pelvis occurred in the group in which thrombosis was not found.

## COMMENT

It is apparent that the evidence of thrombosis found in the specimen examined in this study was secondary to acute appendicitis. This can be concluded from several findings: (1) wherever evidence of thrombosis was found it was minimal and was present in an extremely small fraction of the total number of vessels in each section; (2) the thrombosed vessel were very small; (3) the surrounding inflammatory reaction was no more marked in the immediate vicinity of the thrombosed vessel than in the adjacent area.

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The majority of thrombosed vessels were found in the submucosa. Although the circulation is of the terminal or peripheral type the vessel anastomoses freely.<sup>14</sup> Hoxter and Weintrol, from their experimental studies, commented on the richness and profusion of anastomoses and showed that the blood supply is in two layers of which the richer is the deeper or submucosal layer. The fact that the majority of the thrombosed vessels were in the freely anastomosing submucous layer probably contradicts the notion that the thrombosis was caused by stagnation of the flow of blood. Rather the thrombosis occurred as a result of endothelial damage and extension of the surrounding inflammation.

Thrombosis is thought to occur more frequently in older people. This apparently is not true of thrombosis which occurs in the vessels of acutely inflamed

## THE ROENTGEN DIAGNOSIS OF VOLVULUS OF THE CECUM

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**V**OLVULUS of the cecum is generally regarded as a rare cause of intestinal obstruction. Yet on the basis of incidence alone it is of sufficient importance to be considered in all cases of acute and recurring types of intestinal obstruction.

The first case of volvulus of the cecum was reported by Rokitsansky<sup>1</sup> in 1841. Following that no thorough consideration of the condition appeared until the work of Monteuffel<sup>2</sup> who reported 4 cases in 1898. Faltin, in 1902, collected 79 cases including those just mentioned. By 1913 Bundschuh<sup>3</sup> was able to collect some 110 cases and in 194 Wolfer Beaton and Anson<sup>4</sup> collected an additional 193 cases making a total of 304. Of these 193 cases, 40 occurred in North America. Since that time a few cases have appeared in the literature each year.

Volvulus of the cecum is commonly a disease of young adults, 50 per cent of Corcoran and Sargent's patients being between the ages of 20 and 40 years. Eighty-four per cent of Bundschuh's<sup>3</sup> patients were under 40 years of age and in the series reported by Faltin, 4 per cent were between the ages of 17 and 20 years. Nevertheless, the condition may occur at any age. The youngest case reported was in an infant of 10 months, the oldest one in a man of 89 years. The four cases which we are reporting were all in patients over 60 years of age. Volvulus of the cecum occurs more frequently in males than in females, the ratio being more than two to one. In our own series all of the cases were in males. It would appear from a consideration of the cases reported in the literature that this condition may be the causative factor in approximately 1 per cent of all the cases of intestinal obstruction.

The designation, volvulus of the cecum is misleading as in almost all of the cases a variable amount of the terminal ileum and ascending colon are usually involved. A better term might be volvulus of the right half of the colon. The site of torsion may be anywhere from the cecum to the splenic flexure. The axis of rotation may be transverse, oblique or parallel to the long axis of the cecum and the ascending colon. In most cases the rotation is in a clockwise direction. Here as in other portions of the bowel a rotation of 180 degrees is usually considered sufficient to produce obstruction. Further twisting will lead to strangulation. It is, however, impossible to demonstrate a physiologic volvulus, without obstruction with a rotation of only 180 degrees.

Volvulus of the cecum may result from either an anatomical or functional cause. Usually it occurs only in the presence of an abnormal mobility of the cecum.

## SUMMARY

Histologic study of sections of 100 appendices in cases of acute appendicitis to determine the incidence of vascular thrombosis has been made along with a study of the histories in each case. Thrombosis was found in 26 of the 100 specimens studied. Eighty-seven thrombosed vessels were found; all were small vessels. The thrombosis appeared to be secondary to the acute appendicitis and dependent, to an extent on the severity of that disease.

Evidence from this study suggests that thrombosed vessels would be found in most gangrenous appendices if serial sections were made and examined.

Pylephlebitis that occurs with acute appendicitis may have its origin in a thrombosed vessel of the diseased appendix.

In this series there was no relationship between the presence of thrombosed vessels within the appendix and the postoperative course of the patient.

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collection of gas at the site of the cecum either in the midline or slightly to the right of it. It was necessary, however, to exclude an organic lesion such as a carcinoma. Jacobsen in 1940 stated that the typical roentgenogram of cecal volvulus shows a greatly distended cecum varying in size with one or two commonly two fluid levels shown with the patient erect or in the lateral decubitus position. Fluid levels are also found in the small bowel. The barium enema will stop at the point of torsion and there is generally seen a typical mucosal pattern indicative of twisting. Roentgen findings have been recently reported by Young, Morrison and Wilson.<sup>17</sup>

During the past year we have seen three cases of volvulus of the cecum in which the diagnosis was made preoperatively. In addition we observed one case in 1944 in which the diagnosis was suspected but not established until abdominal exploration was undertaken. On the basis of these cases we feel that the criteria for diagnosis are present in the simple film of the abdomen and that the barium enema is not an absolutely necessary diagnostic procedure although it may be very helpful to confirm positively the suspected diagnosis.

The findings in the simple film of the abdomen are as follows: (1) the cecum is greatly dilated and appears to be in an ectopic position. (2) loops of small bowel may be seen distended with gas, often lying to the right of the distended cecum. (3) the ileocecal valve may be demonstrable lying to the right of the distended cecum; it will give a distinct shadow in contrast with the gas in the cecum surrounding it and in the small bowel within it. (4) the spiral distortion of the mucous membrane folds may sometimes be seen at the site of twisting, being visible because of contrast with the gas in the bowel. (5) there is usually a considerable dilatation of the small bowel with fluid levels seen in the upright position suggesting a small bowel obstruction; this results from the relatively proximal position of the obstruction in the colon. Differentiation from volvulus of the sigmoid, organic obstruction of the transverse or sigmoid colon due to carcinoma and adynamic ileus must be accomplished. Obviously if the site of obstruction can be seen this tends to make the differential diagnosis clear. If the site of obstruction is clearly delineated in the left lower quadrant, volvulus of the cecum can be ruled out fairly well. Usually with obstruction of the sigmoid there is little or no distention of the small bowel. Often the distended loops of sigmoid can be easily identified rising up out of the pelvis either to the right or left and the point of torsion may be seen. In most instances of volvulus of the sigmoid two fluid levels are seen in the upright position.

The utilization of the barium enema is advisable where a serious difficulty in differentiation occurs. When given with care there is little or no danger and the exact site of obstruction, torsion of the colon may well be demonstrated making the diagnosis perfectly definite.

The differential diagnosis from adynamic ileus may present some difficulties. Usually in adynamic ileus one has little or no distention in contrast to the cramps and borborygmi found with obstruction. Roentgenologically in adynamic ileus there is generalized distention of both the large and small bowel but this does not necessarily follow as regular accumulation of gas may occasionally

and ascending colon which is present in approximately 10 to 15 per cent of adults. Such abnormal mobility is a result of failure of fusion or fixation of the posterior cecal mesocolon to the parietal peritoneum of the posterior abdominal wall. Other anomalies which are found with volvulus of the cecum are a long mesocolon and mesocecum, a common ileocecal mesentery, retroperitoneal ileum and malpositions of the cecum including inversion, left-sided position, and reversed rotation.

Functionally both stasis and hyperperistalsis have been predicated as precipitating factors. Other factors frequently mentioned are high residue diet, violent exercise, pregnancy and tumors.

Volvulus of the right half of the colon occurs frequently enough following abdominal surgery to be worthy of particular mention. One of our patients developed the condition subsequent to a subtotal gastrectomy. Other cases have been reported in the literature in which the lesion apparently followed a surgical procedure on the abdomen.

Two clinical types of volvulus of the cecum occur—the acute and the recurrent. The symptoms are those of a true mechanical bowel obstruction with vomiting, abdominal cramps associated with borborygmi, abdominal distention, and obstipation occurring. Physical examination reveals moderate tenderness over the massively dilated cecum which may be found in an ectopic position. Signs of peritoneal irritation are usually absent unless the process has gone on to infarction with peritoneal contamination. The attack may relent spontaneously under nonoperative therapy only to recur again at a later time. In the recurrent type symptoms simulate acute appendicitis and patients have been operated upon under that diagnosis, only to find a volvulus of the cecum at operation.

The preoperative diagnosis of volvulus of the right half of the colon has been made very infrequently in the past. The possibilities of roentgen examination as a means of making this diagnosis have been recognized and in the light of our experience there is no doubt that this may be the most important single factor in determining the presence of the condition.

Roentgen examination of the abdomen in such situations may be accomplished without the use of contrast material. The diagnosis of volvulus of the sigmoid has been reported on many occasions. It is particularly well demonstrated by means of the barium enema, as was shown by Laurell<sup>11</sup> in 1926. He demonstrated the twisting of the sigmoid colon up to 180 degrees by means of the visualization of the mucosal haustra pattern. At the same time he showed that a film of the abdomen, without the use of contrast material, oftentimes will reveal the site of the obstruction and that the mucosal pattern may be delineated in the adjacent bowel by contrast with the gas which is present.

In 1937 Easton and Adams made preoperative diagnosis of volvulus of the cecum by means of a barium enema. They postulated that two conditions indicated the presence of a volvulus of the cecum. The first was an obstruction to the passage of barium by enema at a certain point in the ascending or transverse colon; the second was the simultaneous presence of a large

**Comment**—This case illustrates better than any of the rest the striking and characteristic findings, particularly the malposition of the cecum, the abnormal position of the ileocecal valve and the distention of the small bowel without much distention of the colon. The characteristic findings on barium enema examination are also clearly delineated.



Fig. 1



Fig. 2

**Fig. 3 (Case 1).**—Barium enema examination in the same case. The findings observed in the single film of the ileocecal region shown here. In addition the points of obstruction in the ascending colon is clearly delineated and the dilated ascending membrane folds are seen just above the end of the barium column.

**CASE 1.**—A J. white male, aged 5 years, admitted to the University Hospital on Dec. 20, 1944. Eight hours prior to admission he began to have crampy lower abdominal pains with development of retching but no vomiting. He had had bowel movement on the day of admission and had passed flatus after receiving three enemas before admission. He had long past history of gastric distress since the age of 19. A diagnosis of peptic ulcer had been made in 1932.

In 1939 the patient had left peritoneotomy at which time roentgenogram (Fig. 3) of the abdomen made in the course of an operation of the left kidney showed dilated large bowel on the right side in very peculiar position. The significance of this was not fully appreciated at that time but it was at least from an examination of the films that the abnormal mobility of the cecum in position being high in the right abdomen, was present at that time.



occur. The cecum can usually be seen to be in normal position and fluid levels are much less common. The small bowel does not show the usual haustra turns characteristic of a dynamic type of obstruction but even this is not completely a differential point. The particular factor of a markedly distended cecum without corresponding distention of the remaining portion of the colon should lead at once to the suspicion that there is a real obstruction in the ascending colon rather than an adynamic ileus. The extent of the small bowel distention is usually greater in adynamic ileus than it is in a volvulus.

The following four cases are reported as illustrations of the findings in this condition.

#### CASE REPORTS

CASE 1—D. J., white male, physician, aged 45 years, admitted to the University Hospital Aug. 20, 1946, with twenty years history of duodenal ulcer. An elective gastric resection was done on Aug. 21, 1946, without untoward event. An appendectomy was also done and an unusual mobility of the cecum, as observed at this time. The immediate post-operative course was normal. However, when the patient began to ingest food there was some distention of the abdomen. No vomiting or colic was present but there was lively peristalsis present throughout the abdomen. Bowel movement were minimal or almost absent. The patient was ambulatory and complained very little but the failure to develop normal bowel movement and the distention of the abdomen gave considerable concern.

The first roentgen examination of the abdomen made Aug. 29, 1946 (Fig. 1) just eight days after the operation, showed all of the findings most adequately although there were not recognized at once. A tremendously distended hollow viscus could be made out lying somewhat to the left of the midline in an arch the shape of the cecum and ascending colon. It measured approximately 15 cm. in diameter. In addition, there was a collection of distended loops of small bowel lying to the right of this viscus and extending up to it. Further observation twelve hours later with additional films brought home the fact that the ileocecal valve was perfectly apparent just overlying the spine and it was identified by reason of the gas filled loop of small bowel which remained between the two lips and by the gas which surrounded the valve in the greatly distended cecum. The position of the cecum and ascending colon lying on the left side with the ileocecal valve lying to the right, and the distended loops of small bowel extending to the right of it together with very little gas shown in the remaining colon, gave clear diagnostic evidence of a volvulus. In order to make absolutely certain, a barium enema was done twelve hours after the original examination. The findings as to the gas filled cecum and the small bowel were almost identical as the roentgenogram (Fig. 2) in which the ileocecal valve was even more clearly delineated just to the right of the spine. The barium enema met an obstruction at a point just proximal to the hepatic flexure and the characteristic twisting of the terminal folds was made out from check by the diagnosis of volvulus of the cecum and ascending colon.

A laparotomy was performed and enormous cecum measuring 24 cm. in length and 15 cm. in diameter was found. Although the bowel as visible showed splitting of the cecum from the extreme distention had already occurred so that an excision of the cecum and 70 cm. of the terminal ileum was done and an oblique end to end anastomosis between the ileum and ascending colon accomplished. Before incision decompression incision was necessary was accomplished and several hundred cubic centimeters of fecal material were removed from the small intestine. A Murphy catheter enterostomy in the distal ileum done after the technique of Wangensteen<sup>1</sup> was performed and was brought out through the abdominal wall above the incision. The postoperative course was marked by some distention for the first week. The enterostomy tube was removed at the end of the second week and the patient was discharged completely well on Sept. 21, 1946.

\*By Dr. G. H. Wangensteen.

In 1941 the patient had another attack of hematemesis and melena. In March, 1943, he was admitted to the hospital with history of nausea and vomiting, abdominal pain, and no bowel movements for three days. At that time diagnosis of perforated ulcer was made but operation was refused and the patient subsequently developed right subdiaphragmatic abscess which was drained followed by relatively uneventful convalescence. In January 1944 the patient was again admitted for hematemesis and melena. Because of these numerous episodes of bleeding, some of which endangered the life of the patient, he was readmitted to the hospital in June 1944 and, ulcers of the stomach and duodenum having been found, subtotal gastric resection was done. Postoperatively the abdomen showed marked distention and on one occasion the film of the abdomen showed an enormous dilatation of the cecum which extended well beyond the midline to the left (Fig. 4). A barium enema examination was done on the same day (Fig. 5). There was angulation of the ascending colon with dilatation of the cecum which was considered due to malposition of the cecum and some spasm. Without further treatment the distention gradually receded and the patient was discharged the middle of July 1944.

He had no further difficulty until admission six months later. On this occasion there was moderate distention of the abdomen with visible and palpable mass in the right upper quadrant. Marked tympany present on percussion and bowel sounds were active. A simple film of the abdomen (Fig. 6) revealed the cecum or ascending colon enormously dilated by gas in the right upper quadrant. There was, in addition, marked distention of the remaining portions of the colon and considerable distention of the small bowel. The exact nature of the process was not appreciated. Re-examination made eighteen hours later showed persistence of this tremendous distended loop of bowel and an obstruction of the colon as predicted but the exact nature of the process was not realized until operation. He operated post Dec. 31 1944, at which time the valvula of the cecum was found with the torsion estimated to be 180 degrees. Gangren of the ileocecal already present. A obstructed Micholitz type of externalization with resection of the cecum and right colon was performed. The postoperative course was uneventful except for slight postoperative dehydration. The patient was discharged Jan. 21 1945, and readmitted in March for closure of the decolourary which was done March 19 1945 with an uneventful convalescence.

**Comment.**—This was the first of the patient which we saw and a diagnosis was not made preoperatively although it was appreciated that some marked abnormality of the ascending colon was present. Review of the films indicates that the condition of the coliculus are present namely the cecum partially non-rotated and lying parallel to the transverse colon the tip of it coming beyond the midline to the left side. No doubt intermittent coliculus had occurred and some of the attacks of which the man complained very likely were related to that. It seems likely also that the postoperative difficulties after the gastrectomy in July 1944 arose from a volvulus which, however, restored itself postoperatively. The final event was a complete volvulus with failure of restoration and the characteristic findings shown in the films.

**Case 2.**—H. V. a white male aged 63 years was admitted to the University Hospital March 15, 1941 with history of colic stabbing pain in the abdomen beginning about three days earlier in the focal point about 4 cm. lateral to the umbilicus on the right side. The pain had continued with only brief remissions for three days until admission. The vomiting began on the evening of March 13 and continued in intermittently at frequent intervals since. The last normal bowel movement was on March 14 but small bowel movements had occurred on

Fig 3



Fig 4



Fig 5

Fig 6

Fig. 9

Fig. 10



Fig.



Fig.

Fig. 9 (C)  
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abdominal  
Dorsal view of the  
of the mass  
of obstruction

Fig. 10 (Case 4) - tumor case history: upon examination the mass was found to be in the  
location of the cecum is still shown, but the position is now a bit abnormal. The  
presence of obstruction of the loops of small bowel still remains. The  
examination of the abdominal area in the previous roentgenogram (Fig. 9) had been repeated.  
The patient's symptoms had been relieved to some degree.

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March 15 and 17 th little dates. The past history as of little significance. On physical examination the abdomen was flat; he did complain but was not extremely so. There was rebound tenderness over the entire abdomen. He was tympanitic there were no bowel sounds and other evidence of abnormality. Roentgenogram of the abdomen (Fig 7) was made. This revealed marked distention of many loops of small bow l with gas but an extraordinary dilatation of the cecum such extended up under the liver and right up to the level of the spine. The character of the distention of the cecum together with that of the



FIG 7



FIG 8

best and abdomen shows a rather poor pattern. The right diaphragm is elevated above the cecum or abnormal colon with slight fluid level. The diagnosis is made.

small bowel and the degree of distention of the remainder of the colon led to the diagnosis of probable volvulus of the cecum. A roentgenogram of the chest made (Fig 8) showed changes in the right lung are present, possibly due to an old tuberculous. The right diaphragm is elevated. Beneath the liver could be made out hollow space with fluid level suggesting tremendously dilated cecum containing large quantity of fluid. This served to confirm the previous diagnosis. There was small gas bubble under the left diaphragm and it could not be determined from this one examination whether that represented free gas from a perforation or simply small amount of gas in the colon. A preoperative diagnosis of probable volvulus of the cecum made. Immediate surgery as undertaken and the volvulus involving the junction of the cecum with the ascending colon found. Detorsion was accomplished but the changes in the bow l made it necessary to resect the cecum and ascending colon. Asphylic red to red anastomosis of the ileum to the transverse colon was accomplished. The postoperative course was uneventful and the patient was discharged March 30 apparently well.

Fig 9



Fig 10



Fig 11

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CASE 4—F. T. white man, aged 42 years, was admitted to the Minneapolis General Hospital May 3, 1947 with complaint of pain beginning in the middle of the back and radiating to the flanks, following fall from porch. Otherwise the history was negative. There was tenderness to palpation over the lower dorsal spaces. A bilateral inguinal hernia was present but there was nothing of any further significance. On roentgen examination compression fracture of the bodies of the tenth and twelfth thoracic vertebrae was found. The patient was put on Buck's extension for the fracture of the spine. With ten pounds weight on each leg. Twenty-four hours later he began to develop bilateral distention which naturally thought to be due to a paralytic ileus. Three days later the patient the Bradford frame had to be given up. The distention apparently responded somewhat to enemas and Proctogaine but on May 7, 1947 it again became noticeable. Peritonitis as indicated by tube in the upper periumbilical but the abdomen remained distended. Roentgen examination of the abdomen was undertaken at this time (Fig 9) and an enormous distended loop of bowel could be made out in the right lower quadrant extending all beyond the outline of the abdomen to the left side. Because of the localized character of this distention and its position the possibility of volvulus of the sigmoid was considered. There was present considerable amount of gas in the distal colon and even in the transverse colon so that the diagnosis of volvulus of the cecum was not given sufficient credence. The following morning

barium enema was administered (Fig 10) and the dilated loop of bowel as then demonstrated to be the cecum. A torsion could be made out but it appeared to be only of partial degree. It was evident from the examination that the volvulus had been reduced to considerable extent in the interim. The patient likewise showed some relief of symptoms.

On further questioning at this time it appeared that this man had had similar symptoms on previous occasions whenever he remained in bed for a few days. He was then permitted to become ambulatory and relief of the distention was accomplished. A recurrence of symptoms was followed by another roentgen examination (Fig 11) forty-eight hours later and the cecum could now be demonstrated occupying the hepatic flexure and extending all up under the liver. There was some residual of barium remaining so that torsion had again occurred. On May 13, however, re-examination (Fig 12) showed an apparently normal cecum and ascending colon. The patient left the hospital against advice on May 17, 1947 the abdominal distention having been completely relieved.

*Comment*—Although it can not be proved completely since the patient was not operated upon, this would certainly appear to be a case of intermittent chronic volvulus of the cecum and ascending colon which was spontaneously reduced to a normal situation. The characteristic distention, the appearance and position of the right half of the colon, the history of the patient and the marked changes which occurred under observation all tend to bear out this assumption.

The treatment of volvulus of the cecum is operative. Simple detorsion of viable bowel will correct the situation for the time being but offers no assurance against recurrence which, once an anatomic predisposition exists, is likely to occur. Fixation of the cecum and right colon to the lateral peritoneum has been suggested but is not particularly effective. If the patient's condition allows, resection of the right colon and primary anastomosis

is a reliable treatment of choice. In the presence of

intere is mandatory although a Mckay

is employed in critical cases. Cecostomy which has been utilized in a number of reported instances, is followed almost uniformly by a fatal outcome. Its use is ment used only to condemn it.

## SUMMARY AND CONCLUSIONS

1 Abnormal mobility of the cecum and ascending colon is the anatomic prerequisite for volvulus of the cecum. It occurs in about 10 to 15 per cent of adults.

The incidence of volvulus of the right half of the colon is approximately 1 per cent of all cases of intestinal obstruction.

3 The diagnosis can be made by roentgen examination from the simple film of the abdomen alone but the addition of a barium enema may present helpful, confirmatory evidence.

4 The roentgen criteria are as follows: (1) dilated cecum lying in a very abnormal position; (2) loops of small bowel lying to the right of the distended cecum; (3) the observation of the ileocecal valve lying to the right of the distended viscus may be absolutely diagnostic; (4) a cone-shaped obstruction of the ascending colon with spiral mucosal folds demonstrated on barium enema examination is likewise diagnostic; (5) usually only a single fluid level is present in the colon when upright films are made; (6) the twisted mucosal folds may occasionally be seen in the simple film of the abdomen by contrast with the surrounding mucosa.

5 A differential diagnosis must be made from colic ulcus of the sigmoid, adynamic ileus, and organic obstruction of the transverse or left colon.

6 Four cases of the acute type of obstruction and two of the chronic or recurrent type are presented in detail. In three of these it was possible to make the diagnosis largely on the basis of the roentgen findings.

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# SURGICAL MANAGEMENT OF THORACIC DUCT INJURIES

## AN EXPERIMENTAL STUDY WITH CLINICAL APPLICATION

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**T**RAUMATIC chylothorax is a rare but not an uncommon condition. Trauma to the thoracic duct or its tributaries may be due either to direct or indirect violence or to operative injury.

Shackelford and Fisher (1938) collected 39 cases of traumatic chylothorax from the literature and added two of their own. In an analysis of the causes of traumatic chylothorax in this group there were 1 due to crushing injuries, 8 to bullet or stab wounds, 6 to a fall from a height, 1 from a blow on the chest, 4 to being thrown against the front seat of an automobile, and 1 to hyperextension of the vertebral column. Cases due to operative trauma were not included in their study.

Loe<sup>1</sup> in a recent case report of a bullet injury to the cervical portion of the thoracic duct associated with chylothorax found about 62 cases of traumatic chylothorax recorded in the literature.

Operative injury to the duct with hemothorax or chylothorax is probably of more frequent occurrence than one is led to believe from reports in the literature. The cervical portion of the duct is most frequently injured in operation on the left side of the neck for tumor or enlarged lymph nodes. If unrecognized and not treated, hemothorax will develop. If the pleura is opened, chylothorax may also occur. In injuries to the intrathoracic portion of the duct, chylothorax with its attendant high mortality will occur unless the injury is promptly recognized and treated.

Whitecomb and Reoville<sup>2</sup> (1941) reported a case in which the thoracic duct was inadvertently severed during a right sympathectomy of the Smithwick type for hypertension. The injury was promptly recognized and two silver clips were placed on either end of the divided duct. However in spite of this their patient developed a right chylothorax with pressure and nutritional symptoms and succumbed during the intra-venous transfusion of the aspirated chyl.

Other cases have been reported in which the thoracic duct was injured high in the chest during esophageal resection or other surgical procedures. Simple ligation of the duct at this level was successful.

Injury to collaterals of the thoracic duct probably occurs not infrequently during intrathoracic operative procedures. The presence of chyle is obscured by the sanguineous character of the fluid that collects and is drained from the



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Whitcomb and Neville<sup>3</sup> (1941) reported a case in which the thoracic duct was inadvertently severed during a right sympathectomy of the Smithwick type for hypertension. The injury was promptly recognized and two silver clips were placed on either end of the divided duct. However in spite of this their patient developed right chylothorax with pressure and nutritional symptoms and succumbed during the intravenous transfusion of the aspirated chyle.

Other cases have been reported in which the thoracic duct was injured high in the chest during esophageal resection or other surgical procedures. Simple ligation of the duct at this level was successful.

Injury to collateral left thoracic duct probably occurs not infrequently during intrathoracic operative procedures. The presence of this duct is obscured by the sanguineous character of the fluid that collects or is drained from the

pleural cavity. In a relatively short period of time the tear in the lymph channel will usually become sealed. However, in an injury to a large tributary chylothorax may not clear up for several days.

The symptoms in chylothorax are those due to pressure and loss of chyle. The pressure symptoms may be relieved by frequent thoracentesis. However, the loss of chyle, if allowed to persist, will result in inanition and death. This is obvious when one considers its composition. Sixty to seventy per cent of the absorbed fat is in chyle. The protein content varies from 1 to 6 Gm. per cent with an average of 3 to 4 Gm. per cent. The nonprotein nitrogen, sugar, urea, and minerals are similar in amount to those found in blood serum. However, the calcium and cholesterol content are slightly lower. The lymphocyte and eosinophile count are much higher than in the blood.

The flow of chyle is at a rate of 50 to 100 cc. per hour and will depend on the fluid intake and diet. Thus, the loss of chyle in a twenty-four hour period may exceed 2,000 cc.

With the loss of these constituents a marked deficiency state develops characterized by weakness, hunger, intense thirst, emaciation, apathy, and death which is due to starvation. The lymphocyte and eosinophil blood count are reduced.

Treatment of chylothorax has been medical, surgical, or combined. In the medical management a proper diet low in fat and rich in protein and vitamins is given. Blood transfusions, plasma, glucose saline solution, intravenous infusion of aspirated chyle, and thoracentesis have been employed. These supportive measures may maintain the patient's nutritional status until spontaneous or operative repair of the injury is carried out.

In operative injuries it is paramount that the injury be recognized at the time and appropriate treatment carried out. Various methods of management have been advocated. As early as 1903 Deenaday had coated implantation of the severed duct into a near-by vein. He successfully implanted the cervical thoracic duct which was severed during removal of tuberculous lymph glands into the left internal jugular vein. Harrison in 1916 implanted the divided cervical thoracic duct into the left external jugular vein. He advocated this as the most physiologically sound method when suturing of the duct is impossible. Ligation or packing is resorted to if the other method cannot be successfully carried out.

In injury to the thoracic portion of the duct, unless in the upper part where there is rich collateral circulation, ligation may be followed by rupture due to the increased intrathoracic pressure brought about by acute obstruction. A safer method must therefore be used since the surgical mortality in traumatic chylothorax has been reported to be around 100 per cent and about 50 per cent in the over-all total cases reported (Loe<sup>3</sup>).

With recognition of the seriousness of this condition and the associated high mortality, experiments were carried out to study and find a rational method of surgical management.

## METHOD

A group of twelve large healthy dogs was used. All were operated upon employing endotracheal positive pressure ether anesthesia. The thoracic duct was approached through the right tenth intercostal space. After entering the thoracic cavity the mediastinal pleura was incised above the diaphragm. The duct lying over the vertebral column and posterior and slightly to the right of the aorta was easily identified. It was then dissected out to the level of the external chyli. Just above the diaphragm the duct was usually found to be a large small trunk with occasional small collaterals. About 6 cm. from the diaphragm relatively large collateral lymphatic trunks were found.

In six animals a 3 cm. segment of the thoracic duct was excised just above the diaphragm. In all there was immediate chylothorax. The mediastinal pleura was left open and the lung re-expanded. The chest incision was closed with layers with catgut and the skin was closed with silk.

In three animals the thoracic duct was ligated with silk at the level of the diaphragm and 4 to 5 cm. above. The segment of duct between the ligatures was then excised.

In another three animals a small segment of the thoracic duct at the level of the tenth thoracic vertebra was excised and the proximal thoracic duct just above the diaphragm was implanted into the azygos vein which is in close relationship. The technique will be described later.

## RESULTS

In the six dogs in which a segment of the thoracic duct was excised and the divided ends left open, four recovered and two died one in forty-eight hours and the other in six days. Both had a massive right chylothorax and developed symptoms due to pressure and loss of hyle. Autopsy was done in two weeks in the four that recovered. Examination disclosed moderate fibrosis about the thoracic duct which was sealed and there were numerous dilated lymph channels. All four animals had evidence of lympho-cystic anastomoses with the azygos and intercostal veins.

In the three animals in which a segment of the thoracic duct was excised and the end ligated recovery was uneventful. Autopsy two weeks later revealed dilated collateral lymph channels but no lympho-cystic anastomoses. There was slight fibrosis about the divided ends of the duct.

Two of the three animals in which a segment of the thoracic duct was excised and the proximal stump implanted into the azygos vein made an uneventful recovery. At autopsy two weeks later disclosed patency of the communication.

The third animal died in the sixth postoperative day and at autopsy an empyema and bilateral pneumothorax were found. The anastomosis between the thoracic duct and azygos vein was patent.

## DISCUSSION

It is interesting that in the first group of dogs in which a segment of the thoracic duct was excised recovery occurred in two-thirds. Closure of the

open ends of the duct and collateral channels and lymphovenous anastomoses developed. Smith and Wolf<sup>10</sup> reported a case of traumatic chylothorax following resection of the entire tenth rib and associated muscles for Ewing's sarcoma of the rib. At operation chyle was noted near the vertebral border but the thoracic duct was not visualized. Pressure symptoms developed on the third postoperative day and on the fifth day thoracentesis was carried out with aspiration of 900 cc of chyle. In the following twelve days 7,800 cc of



Fig. 1.—The dilated thoracic duct being prepared for implantation into the azygos vein which is in close proximity.

chyle were removed in five thoracenteses. On the fourteenth day there was no further accumulation of chyle. In this case healing occurred. However it is quite possible that a large tributary of the thoracic duct or a part of the wall was injured without complete severance of the main duct.

Simple ligation of the thoracic duct at any level in the dog is usually followed by no untoward effects. Blacklock and associates<sup>11</sup> and Lee<sup>12</sup> have shown that it is extremely difficult to obtain complete lymphatic blockade in experimental animals. In man ligation of the duct in the cervical and upper thoracic portion has been successful. However in ligation of the lower third where the

collateral circulation is not as rich as in the upper rupture may occur from a high intraductal pressure brought on by the acute obstruction.

It appears that in injuries of the lower part of the thoracic duct ligation is unsafe. If a primary repair of the injured or severed duct cannot be accomplished, then implantation of the thoracic duct into the axilla or other suitable vein should be carried out. This treatment appears to be the most physiologic if primary repair cannot be accomplished. We have successfully carried out such a procedure in a patient in whom the thoracic duct was inadvertently severed during the course of a transthoracic thoracolumbar sympathectomy for hypertension. The case will be presented in more detail.

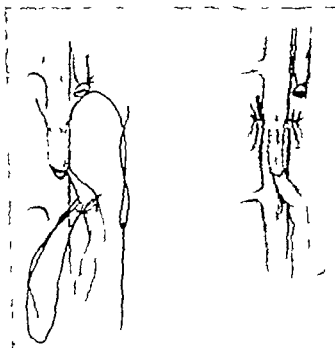


FIG. 2.—Technique of implantation of thoracic duct into the axilla.

#### CASE REPORT

L. D. (Bridges), 41, well married man, was admitted to Duke Hospital on July 4, 1944, with chief complaint of high blood pressure of fifteen years duration. He had done well until three years previous to hospitalization when the headaches became more severe and also began an irregular blurring of vision at times. The blood pressure was 160/125.

After complete examination sympathectomy was recommended. On Aug. 15, 1944, left transthoracic thoracolumbar sympathectomy, apicectomy, and retractor myotomy were carried out. The postoperative course was unremarkable. On Aug. 29, 1944, the second stage was carried out on the right side. The sixth rib was resected and the thoracic cavity entered. After the lung was retracted the mediastinal pleura was incised along the course of the sympathetic chain which was resected from the fifth thoracic to the second lumbar ganglion.



In dissecting the major splanchnic veins the thoracic duct was inadvertently torn with the prompt escape of chyle. The sympathectomy was completed. It was impossible to reconstruct the severed thoracic duct by primary anastomosis. The alternatives were to ligate the duct, to transplant it into the venous system posteriorly or to ligate the duct into the vein. The latter seemed more desirable and the axillary vein was selected.

Five silk sutures were then placed on either side of the thoracic duct using straight intestinal needles (Fig. 1). The axillary vein was then ligated close to the diaphragm. The intercostal vein just below a double ligated and divided. A traction suture was placed around the axillary vein just below the entrance of the next intercostal vein to prevent bleeding. As packing was then made into the venous space of the diameter of the thoracic duct. The intestinal needles were then passed up the vein and out on either side and the duct pulled into the vein for a distance of about  $\frac{1}{2}$  cm. The sutures were then anchored to the surrounding tissues (Fig. 2). The chest was closed in layers. A peccor catheter was placed in the sixth intercostal space in the posterior axillary line for drainage.

The postoperative course was smooth and unremarkable. At no time did the patient show evidence of chylothorax or nutritional deficiencies. During the first week the fat content of the duct was restricted. She was discharged from the hospital on the fourteenth postoperative day with a blood pressure of 120/70.

#### SUMMARY AND CONCLUSIONS

The problem of traumatic chylothorax has been reviewed.

Experiments have been reported in which successful transplantation of the thoracic duct into the axillary vein has been accomplished.

The clinical application of this method has been carried out in a case of operative injury to the thoracic duct. This method is not only applicable to those cases of traumatic chylothorax but may be of value in chylothorax due to obstruction from various causes (tumor inflammation, thrombosis of subclavian vein etc.) in the upper mediastinum.

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mm glass tubes. In heparinized blood, the red cells and plasma separate to form two distinct layers, and the end point is read at the moment of coagulation of the red cells.

On the first day of the experiment the heparin tolerance test alone was performed. On the second day the heparin tolerance test was repeated one-half hour after Caronamide was administered in either of two ways: (1) 2 Gm orally every three hours for six doses or (2) a single 4 Gm dose. The peak of Caronamide blood level occurs approximately one-half hour after an oral dose.<sup>14</sup> No more Caronamide was given at any time during the experiment. The 25 or 50 mg tolerance test (as the case may be) was then repeated once daily until the coagulation curves returned to normal.

Protamine sulfate titrations of heparin levels were performed simultaneously with the coagulation times on the last seven patients. Prothrombin determinations were made on alternate days.

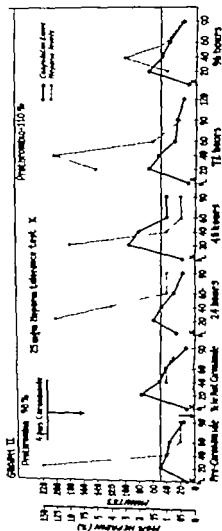
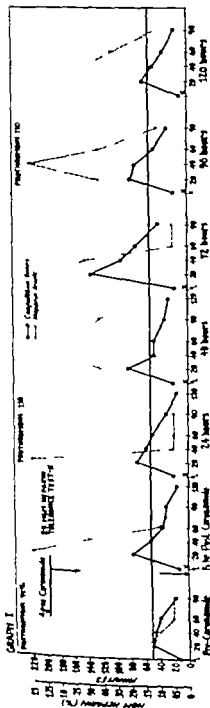
#### RESULTS

*Maximum Response* (five patients).—Graph I illustrates the results obtained from one patient of this group. In all patients in this category the coagulation time of the 20-minute sample of the peak day was prolonged three to ten times that of the corresponding sample of the pre-Caronamide control. It should be noted that the blood sample drawn at 20 minutes always has the longest coagulation time; the times of that sample become gradually more prolonged on successive days until a peak is reached 72 hours after the last dose of Caronamide. This is followed by a gradual decline of the peaks to normal. In three patients of this group the coagulation times of the 20-minute sample were six to ten times more prolonged at the peak period than those of the respective point on their control curves. This patient represents the smallest response of this group.

*Intermediate Response* (three patients).—Graph II illustrates the results obtained from one of these three patients. The coagulation time of the 20-minute peak period sample as compared to the control curve was only doubled. The fact that in this patient the peak was at 48 instead of 72 hours may be of no significance.

*Minimal Response* (two patients).—Graph III. Even though the coagulation time of the 20-minute sample of the peak period (which occurred 120 hours after the last dose of Caronamide) reached 4 hours, it was only 30 minutes longer than the pre-Caronamide control curve. However, it will be noted that the 40-minute sample is almost twice the respective pre-Caronamide coagulation time. This individual is apparently a hyperreactor to heparin and, therefore, is not strictly comparable to the other individual.

*Group Averages* (all ten patients).—Graph IV is a composite graph of the averages of the coagulation times of all ten patients for each period. The curve clearly demonstrates the predominance of the 72-hour peak, the gradual rise in the coagulation time in the first 48 hours, and the more rapid decline to pre-Caronamide response 120 hours later. At the peak period, coagulation times are approximately three times longer than the pre-Caronamide levels in all except



Graphs I to IV courtesy Otsu Nat. Lab. Faculty Department of Microbiology

mini glass tubes. In heparinized blood the red cells and plasma separate to form two distinct layers, and the end point is read at the moment of coagulation of the red cells.<sup>12</sup>

On the first day of the experiment the heparin tolerance test alone was performed. On the second day the heparin tolerance test was repeated one half hour after Caronamide was administered in either of two ways (1) Orally every three hours for 12 doses, or (2) a single 4 gm dose. The peak of Caronamide blood level occurs approximately one-half hour after an oral dose.<sup>13</sup> No more Caronamide was given at any time during the experiment. The 25 or 50 mg. tolerance test (as the case may be) was then repeated once daily until the coagulation curves returned to normal.

Irotamine sulfate titrations of heparin level were performed simultaneously with the coagulation times on the last seven patients. Prothrombin determinations were made on alternate days.

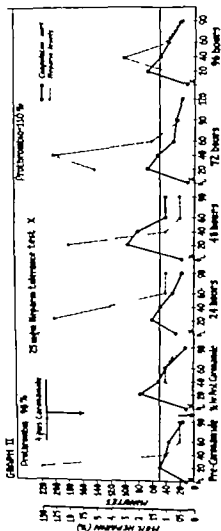
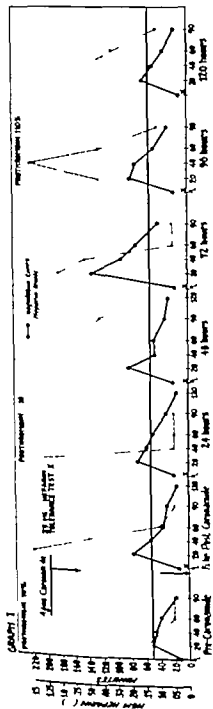
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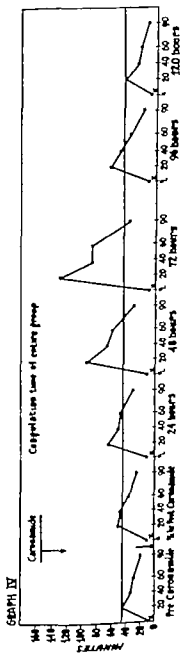
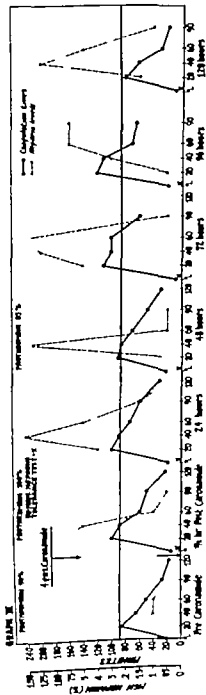
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Graphs I &amp; II courtesy Ohio State University Department of Hematology



the 90-minute sample. The coagulation times of the 48-hour period are twice those of the base line levels; those of the 24- and 96-hour periods are just slightly less than double.

*Heparin Levels*—In reviewing all the graphs, the heparin levels were noted to show no typical pattern either by comparison of the curves of the same patient on successive days of the experiment or by comparison of all the patients' curves for any one particular period. Some of the levels were highest at the 20 minute drawing; others peaked at 40 minutes. Some curves fell abruptly to normal after the peak; others declined gradually. The averages of the heparin levels of all ten patients were plotted in a curve similar to the one in Graph IV. It was not considered significant because of its lack of correlation to any individual case.

It would seem that these small doses of heparin produced a maximum effect within a few minutes after injection and then were rapidly eliminated in the course of one hour (see Graphs I, II and III). There appears to be another factor other than the titer of heparin itself in producing such an enhancement of the coagulation time. In each of several patients, at the same period that the coagulation time was increased six to ten times those of the control time, the heparin levels of both periods remained comparable.

*Prothrombin Determinations*—At the beginning of the experiment and on alternate days thereafter, prothrombin determinations were performed from blood samples drawn prior to the injection of heparin for that day. The per cent of prothrombin determined before the experiment was within normal limits in all patients. In no case were they depressed significantly after Caronamide-heparin administration. On the contrary, in four patients the per cent of prothrombin actually rose during the experiment. This response is perhaps not the result of an increase in prothrombin but rather of some fundamental alteration in the clotting mechanism.

*Comparing the Time Relationship of the Administration of the Two Drugs*—A group of three patients was given 0.5 gm. of Caronamide every 3 hours for 6 days; the last dose was followed in one-half hour by a tolerance test of 25 mg. of heparin. When these individuals failed to have the same response as the others, investigation revealed that at 3 hours had elapsed between the last dose of Caronamide and the intravenous heparin. Four days later the same patients were given a single 4 gm. dose of Caronamide and one-half hour later 25 mg. of intravenous heparin. This time they responded in the same fashion as the previous group. This incident suggests that the single dose (or the last of multiple doses) of Caronamide is the important one and that the heparin must be given at the proper interval following it in order to initiate the process.

#### DISCUSSION AND CONCLUSION

It has been demonstrated in the foregoing that Caronamide administered in a single 4 gm. dose or a course of multiple doses, markedly increases the effect of heparin on the coagulation time of human blood. Of ten patients, eight had a response resulting in a prolongation of the coagulation time (roughly a peak response approximately 7 hours after the administration of Caron-



amide) of two to ten times greater than pre- $\beta$ -arionamide levels. This increase in coagulation time is present to a lesser extent at the 40- and 60-minute drawings. In a few instances, a marked increase in the total length of heparin effect occurred.

I previous mention has been made of the two different methods of administering Caronamide and the results have demonstrated that there is no appreciable difference when either method is employed. However we believe that it is most important to give the last of multiple doses of Caronamide (or the single dose) one-half hour prior to the administration of the heparin. Evidently in order to obtain a maximum result from Caronamide-heparin, the optimum blood concentration of each must be present simultaneously.

Unpublished data concerning urinary excretion of heparin made during the course of these experiments, the implication of the rapid fall of the heparin blood levels, and the progressive daily enhancement of the heparin effect suggest that the results are not solely due to altered renal tubular function. For this reason, two theories have been postulated to explain this phenomenon. One of us (H.D.S.) feels that a new compound is formed which exerts a reversible inhibitory effect on the site of production of the anti-heparin in the body. Charles and associates have isolated a substance with an anti-heparin property deriving from the tissues of preparation of heparin from lung tissue. If the new compound acted upon the circulating anti-heparin itself rather than the site of its production, then one might expect the response on the first day to be higher than those of the succeeding days. The pattern of the curves on Graphs I to IV demonstrates the converse—the least response on the first day with a progressive rise of the curve on succeeding days. With each successive dose of heparin, the already present circulating anti-heparin is consumed, so that by the third day for example the titer of anti-heparin is least. Finally when the titer of anti-heparin is lowest the injected heparin is relatively unopposed and produces the longest coagulation time. The return to normal on the day following the peak period would be a manifestation of the gradual recovery of the mechanism which produces the anti-heparin. This progressive daily increase in coagulation time response to heparin is somewhat analogous to the delayed action of benzoinol and rising prothrombin level.

The other theory (R.G.M.) also postulates that a new chemical compound is formed. This is suggested by the necessity for the close correlation of blood level peak of Caronamide and heparin to establish the gradually increasing enhancement of heparin activity. The fact that the maximum response is obtained after approximately 72 hours indicates the possibility that the compound thus formed may increase quantitatively by autoreproduction. Nucleofolins are

Caronamide and suggest that the blood level of heparin is maintained. Although the strong negative charge of heparin from the sulfate ions present.

makes the formation of a nucleic-acidlike compound less probable than if phosphate ions were present it is considered chemically possible for such a compound to be formed. Earle and Brodie<sup>8</sup> have shown in dogs that 59 to 68 per cent of Caronamide is bound on plasma proteins. In addition, with the known proclivity of heparin to form complexes with plasma proteins,<sup>20, 21</sup> a compound not unlike a nucleoprotein in characteristics or capability may be formed when plasma proteins, heparin and Caronamide are united *in vivo*. If such a compound were formed, and increased in quantity it could call forth its own antagonist and thereby be gradually decreased in activity or excreted in the urine. Such a compound would then act either synergistically with newly injected heparin in such a manner as to increase its anticoagulant effect, or antagonistically to a physiologic anti-heparin. This theory is also partially suggested by the fact that the base line coagulation times and protrombin times do not increase and therefore such a compound appears not to have a measurable effect on the physiologic balance maintaining normal coagulability. Experiments are under way to attest or improve these theories.

At present the cost of heparin and the difficulty in maintaining an adequate prolongation of the coagulation time detract considerably from its usefulness in the treatment of thromboses. Heparin in Pitkin menstruum has provided a better means of administering a therapeutic course but this method still has some undesirable features. It is hoped that the studies<sup>22</sup> of Caronamide with heparin in Pitkin menstruum now in progress, may provide a better solution to the problem of heparin therapy. The fact that the results described in this paper can be achieved with such small doses of heparin makes the outlook appear promising for reducing the cost of heparin therapy. Further studies with oral and intravenous Caronamide in combination with aqueous heparin and heparin in saline solution administered by various routes are also in progress.

# SUMMARY

1 Intravenous heparin in saline solution, given one half hour after a single dose of Caronamide causes a progressive enhancement of the effect of an equal dose of heparin administered on each successive day.

In eight of ten patients, this enhancement reached a peak in approximately 3 days and is manifested by a ten to tenfold increase in coagulation time response to heparin.

2 This peak is followed by a gradual return to a normal response 2 to 3 days later.

4 Incomplete evidence suggests that this effect may be due to the formation of a new compound and not to Caronamide blockage of the renal excretion of heparin.

The fact that the results described in this paper can be achieved with such small doses of heparin makes the outlook appear promising for reducing the cost of heparin therapy.

Acknowledgment: The authors wish to express their appreciation to Miss Leticia Pacheco for her technical assistance.





plet intestinal obstruction (stair anal ex revealed marked decrease in total acidity with absence of free acid. The patient was given nasogastric tube for the relief of this discomfort and when admitted to the hospital she was taking codeine and morphine frequently. On admission to the hospital the patient showed marked anemia, 2,500,000 red blood cells, 6.5 hemoglobin, 4,100 white cells, and normal differential count. She was given three transfusions this week with no appreciable change in the hemogram. She was then given 25 mg folic acid daily and immediate response occurred. In one month the erythrocyte count rose to 4,500,000 and the hemoglobin to 12.5 Gm. The diarrhea and pyrexia disappeared, and the patient gained weight.

TABLE I. LAMINGTON F. IN CASE (H. C.) BEFORE AFTER TREATMENT WITH FOLIC ACID

DATE	H. C. (M)	W	H (Gm)	PCV (%)	SPERMATOCYTES (M)	THERAPY
						REPORT ADVERSE 6 transfusions past month
10/29/46	3	5,100	7.1		Less than 0.1	
11/ 8/46	2	2,750	9.45			AFTER UNITS 7 transfusions Iron and vitamins Folic acid only 25 mg daily
11/11/46	20			10,000		
14	704	4,200	8.9		3.0	
18	34	9,200	10.3	400,000	14.0	
22	4.13	4,100	11.6	500,000	10.8	
26	4.74	14,230	11.6	179,000	2.9	
1- 2/46	4.08	5,400	1.6		7.0	
6	4.8	4,700	1.6	14,000	1.8	

Mrs. F. J. aged 51 years, was diagnosed as having carcinoma of the cecum and ascending colon in 1937. At this time she had blood count of 1,800,000 with marked hypochromic anemia. A one-stage ileocecal resection was performed with resection of the cecum, ascending colon and portion of the terminal ileum. The patient did well postoperatively except for persistent anemia. She showed no evidence of recurrence of the carcinoma for this ten year period. She was given large quantities of iron and liver with little improvement. The improvement however temporary and the anemia returned. As the treatment was discontinued at no time did the anemia disappear completely. The administration of folic acid began March, 1946 concomitantly with iron and liver and marked rise in the erythrocyte count and hemoglobin resulted. At the present time there is no evidence of hypochromic anemia. The red count is approximately 4,000,000 and the hemoglobin 10 Gm.

In 1890 Whit described a series of thirty-one cases of pernicious anemia in which six patients at autopsy had macroscopic lesions of the gastrointestinal tract. In two of these there were ulcerative changes in the ileum. Faber in 1895 described a case of pernicious anemia in a young woman, with fibrous thickening in the wall of the distal part of the jejunum and stricture formation demonstrated at autopsy. He suggested at this time that the anemia resulted from the absorption of toxin from the stagnant bowel contents.

Mikulicz in 1921 observed that primary tuberculous stricture of the ileum in a case of severe pernicious anemia, and also found that the entire small intestine was heavily infected with bacteria. On reviewing this case and similar ones, he concluded that (1) pernicious anemia may develop on the basis of benign intestinal strictures (2) the anemia was probably due to the absorption

of hemotoxic substances from the dilated and infected portion of the bowel above the stricture. (3) such cases support the theory of the intestinal origin of cryptogenetic pernicious anemia.

The work of Castle and his group<sup>10</sup> in 1929 to 1930, has done much to clarify the etiologic basis for pernicious anemia and other similar macrocytic anemias. In order to understand the gastrointestinal relationship it is necessary to review the process by which red blood cells are developed and released to the peripheral blood. An unidentified substance, the extrinsic factor is in food in the diet and this react with an intrinsic factor probably an enzyme which is contained in the gastric secretions. The substance which forms a product of this interaction controls the rate of formation of red blood cell in the bone marrow. Thus, since red cells are not normally released until maturity, a disturbance anywhere in this process will result in a diminution of the number of red cells released to the peripheral circulation, and anemia will then develop.

Goldhamer<sup>11</sup> has shown that pernicious anemia is due to a diminution of the intrinsic factor. Sturgis and Goldhamer<sup>12</sup> believed that the anemia in stricture and anastomosis of the intestine may be due to a failure to absorb the substance which results from the interaction between the extrinsic and intrinsic factors. Kravke<sup>13</sup> however has shown that this substance may be stored, synthesized, and released in the kidney and in other tissues.

Rytis<sup>14</sup> in 1927, Glatzel<sup>15</sup> in 1929 and Sturgis and Goldhamer<sup>12</sup> in 1939 each reported a case of hyperchromic macrocytic anemia following resection of small intestine. In each of these cases, after four, five and five years, respectively, the patient developed a hyperchromic or macrocytic anemia, and a hypochylia or an achylia. Other reports of extensive resections of the small intestine have been made but contain no conclusive information regarding the blood picture.

Terminal ileitis is also rather frequently accompanied by a hyperchromic macrocytic anemia. Plum and Warburg<sup>16</sup> have reported four patients in whom this condition occurred, three of whom had a hyperchromic anemia. They found a much lower incidence of hyperchromic anemia in a series collected from the literature. Butt and Watkins<sup>17</sup> reported upon seven patients with ileitis, six of whom had a macrocytic anemia. None of these patients were benefited by liver therapy but there was recovery with operation. In the series of Plum and Warburg, two of the three patients developed a normal blood picture after liver therapy. They considered the anemia on a deficiency basis.

Darker and Humm<sup>18</sup> studying macrocytic anemia in association with intestinal strictures and anastomoses, collected forty-nine cases from the literature to which they added two of their own. They found macrocytosis in forty-eight of forty-nine and hyperchromia in thirty-two of forty-two. They considered the most plausible explanations for the development of this anemia to be (1) failure of formation of the hemopoietic principle or destruction of the principle in the gastrointestinal tract through abnormal bacterial activity and (2) the absorption of toxic product of bacterial putrefaction in amount too great to be neutralized by the normal detoxifying mechanisms of the body. They believed that instead of regarding the active principle of the liver as being an

erythropoietic substance, it may be necessary to promote detoxification of some chemical compound or compounds, which if unneutralized might lead to a variety of harmful changes throughout the body. The macrocytic anemia resulting from strictures would thus be an intestinal toxemia, which could be alleviated by removing the cause of the stagnation and putrefaction of the intestinal contents, or by administering excessive amounts of the liver principle in order to detoxify the excess of toxins absorbed.

In 1941 Petri, Norgaard, and Jensen<sup>10</sup> reported a series of experiments in which they attempted to produce a condition simulating pernicious anemia in dogs. Sharpe, McLean and Hilde<sup>11</sup> and Meulengracht had previously reported the degrees of effectiveness of different parts of the stomach and duodenum of wine in the treatment of pernicious anemia. Thus, Petri and his group performed resections of the stomach and duodenum in varying combinations in an effort to eliminate the intrinsic factor. These procedures constantly resulted in the production of a chronic subpellagra or an acute or chronic pellagra, but only two of twenty-five animals developed hyperchromia.

Petri and his group then extended their combined resections to include also the distal two-thirds of the small intestine. In doing this they attempted not only to eliminate an assumed site of formation of the intrinsic factor but in addition they believed that they would remove an essential portion of the area in which presumably the interaction between the intrinsic and extrinsic factors is referred. This might in addition, eliminate the site of absorption of the active principle. All of the animals developed an achylia, and two of three developed a hyperchromic macrocytic anemia. All developed skin and central nervous system changes, but the bone marrow was hypoplastic rather than of the hyperplastic type seen in pernicious anemia. The condition thus resembled sprue, minimal ileitis, tropical macrocytic anemia, idiopathic steatorrhea, and fish tapeworm infestation.

Petri and his group<sup>10</sup> then attempted to find exactly what part the resection of the distal small intestine had played in the production of the pathologic picture observed in the combined resections. They resected the distal 81 per cent, 60 per cent and 63 per cent of the small intestine of three pups. In each of these a hyperchromic, macrocytic anemia developed, beginning between seventy-five and ninety-one days postoperatively. They concluded from these experiments that isolated resection of the small intestine produced fundamentally the same type of endogenous pellagra as distal resection of the pylorus and Brunner gland area of duodenum and distal two-thirds of the small intestine and as resection of the pylorus and Brunner gland area of the duodenum. The hyperchromic macrocytic anemia, hypoplasia of the marrow and diarrhea constitute a specific enterogenous phenomena in that they were not seen after resection of the pylorus and Brunner gland area of the duodenum alone. Yet they appeared of the same nature or even accentuated by isolated resection of the small intestine.

Viewing the results of these experiments in the light of clinical observations, it would seem that this type of anemia is due to faulty or absent absorption or

production of substances that ordinarily counteract macrocytosis and hyperchromia, namely antipernicious anemia factor and vitamin B. Or according to Petri, they may be attributed to a possible toxic effect on the liver and bone marrow that is related to the chronic state of diarrhea which is present in this condition.

In an attempt to produce a hyperchronic macrocytic anemia in experimental animals, massive resections of the small intestine were performed in adult dogs. This was done to determine if the same results obtained by Petri in puppies could be produced in older animals, and to enlarge the number of animals in which a surgical anemia had been produced. It was also believed that these animals would lend themselves well to the study of various therapeutic methods, particularly folic acid.

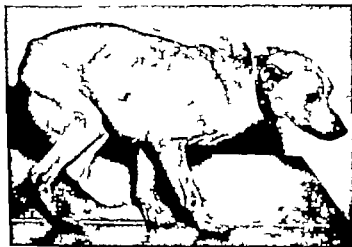


Fig 1.—Photograph of dog shows extreme malnutrition and ulcerations on trembles following resection of the small intestine.

#### EXPERIMENTAL PROCEDURE

Adult dogs were used, the weight averaging 9 to 1 kilograms. After anesthesia had been obtained with intravenous administration of 64 mg of sodium pentobarbital per five pound body weight, the animal was subjected to laparotomy under aseptic technique. Mass resection of the small intestine was performed leaving in each instance approximately four to five inches of proximal jejunum and the same length of terminal ileum. End-to-end anastomosis was done using chromic catgut for mucosa and muscular layers and fine black silk for serosa. The abdomen was routinely closed without drain.

In some instances, parenteral fluids were given for three to five days postoperatively to restore fluid balance. Water was allowed by mouth immediately but no food for three or four days. A standard diet of raw meat and dog biscuits was then offered. Hemoglobin and water intake were recorded frequently.

Blood samples were obtained from the femoral vein preoperatively and at various intervals postoperatively.



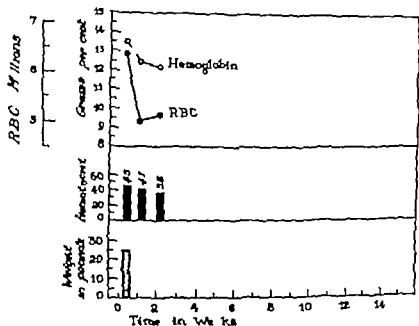


FIG. 1.—Chart demonstrating time the drop in blood counts and hemoglobin in the experimental animal follows the resection of the intestine.

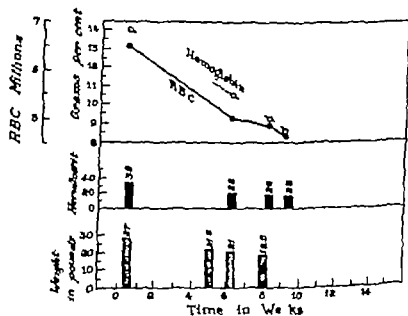


FIG. 2.—Chart of blood counts in an animal showing marked drop but over a longer period following resection of the intestine.

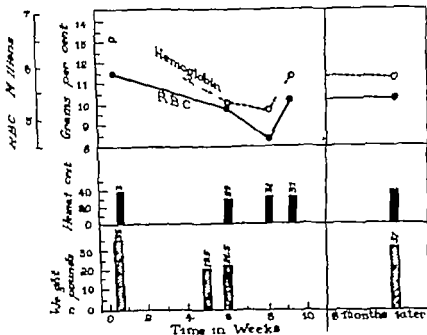


Fig 4—Chart showing the characteristic early findings and also late findings following resection of the small intestine. It is noted that at the end of eight months the blood count is normal on a diet of 1000 calories.

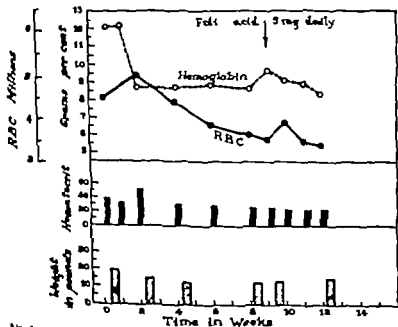


Fig 5—Chart showing the failure of the correction of the anemia induced by intestinal resection in the demonstration of folic acid.

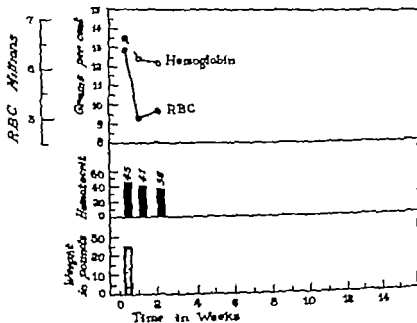


Fig. 2—Chart demonstrating the drop in blood count and hematocrit in the experimental animal following the retention of the infection.

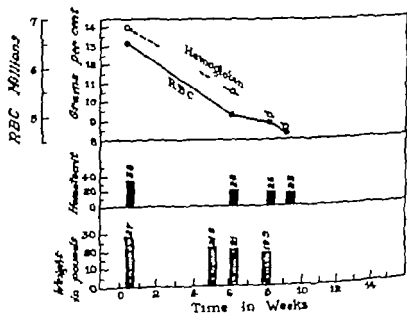


Fig. 3—Chart of blood counts in animal showing marked drop but after some period following infection of the infection.

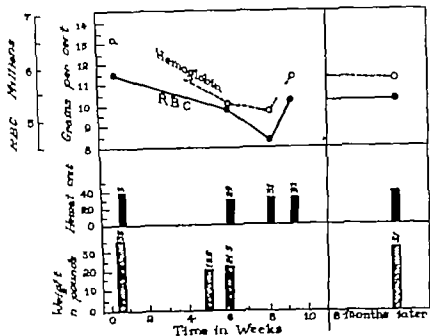


Fig 4—Chart showing the characteristic early findings and late findings following resection of the small intestine. It is noted that at the end of each month the blood count and hemoglobin are (this normal) found on usual diet.

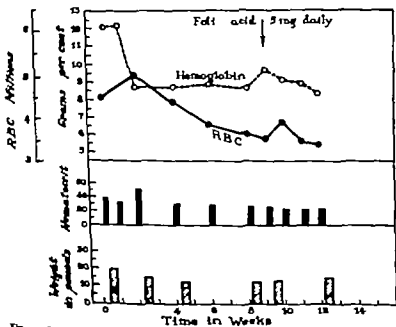


Fig 5—Chart demonstrating the flare of the anemia professed by infections are resolved by the administration of folic acid.

Erythrocyte count were made; hemoglobin content was read from the Sanford-Sheard photometer and hematocrit was determined by the Wintrobe method. Wet and permanent preparations stained with brilliant cresyl blue for reticulocyte count were made and these reported as per cent after a count of 1,000.

#### RESULTS

Of twelve animals having massive resections, only four survived a sufficient length of time for study. A majority of the postoperative deaths occurred in the first seven to ten days following resection and were due to dehydration and malnutrition. Autopsy revealed no deaths due to peritoneal infection or leakage of the anastomosis.

In the animals which survived for a month or more, a characteristic pattern of events was noted. At first hemoconcentration occurred due to dehydration from diarrhea and low fluid intake. After adequate fluid intake was resumed, approximately normal counts were obtained. Three to four weeks postoperatively, however, red cell count and hemoglobin began dropping progressively to low levels, at which they were maintained. Reticulocytes were extremely low or absent. (The normal reticulocyte count for the dog is 3 to 5 per cent.) Weight began to decline postoperatively and after a 30 to 40 per cent reduction, remained fairly stable. The animal took on the appearance of chronic malnutrition, and one of them particularly showed a characteristic loss of hair over the extensor surfaces and head, with skin changes similar to those seen in pellagra.

Changes in volume and color indices were not constant, and no definite trend toward macrocytosis could be established. Present in all, however, was the marked lowering of hemoglobin and erythrocyte count, with low reticulocyte counts.

No response was noted in the animals treated with folic acid, 5 mg. daily by mouth. Most of the animals retained good appetites and consumed normal or greater than normal quantities of food passing large semiformal light-colored stool.

#### CONCLUSION FROM EXPERIMENT

Massive resection of small intestine in the adult dog produces a marked state of malnutrition with a resultant anemia. This anemia is not constant as to type. Lack of significant changes in color indices would seem to indicate that iron stores were adequate. Iron taken in the diet as myoglobin and hemoglobin was adequate to prevent iron deficiency. Also, adequate amounts of proteins were given in the diet, but not absorbed.

The anemias of the state produced in the experimental animal does not lend itself well for comparison with clinical cases, inasmuch as the time intervals involved are different. Lack of response to folic acid suggests that the severe anemia produced in the animal is not entirely upon the same basis as that in the clinical case. Perhaps more restricted resections over longer intervals might more nearly produce anemias of a macrocytic type which would show response to folic acid.



# EFFECT OF ABSORBABLE SPONGES ON INFECTION

## EXPERIMENTAL STUDY

ARTHUR F. CIPOLLA, M.D. AND JOSEPH K. NARAY, M.D. CHICAGO, ILL.

AN ABSORBABLE agent for hemostasis was first employed by Cushing<sup>1</sup> in the form of a trip of muscle tissue. Grey 1913 and Harvey 1916, introduced fibrin for the same purpose while fibrin foam was recommended by Ingraham and Balle. The employment of absorbable material for hemostasis was placed on a practical basis since the introduction of synthetic materials such as oxidized cellulose (Unruh and Kenyon) and gelatin (Correll and Wase). Numerous investigators confirmed the value of such products for hemostasis in various fields of surgery. The popularity of the absorbable sponges suggested the question whether the presence of infection should be considered a contraindication to their use. We attempted to study the problem in the following manner. A culture of pathogenic microorganisms was implanted into subcutaneous pockets in dogs, and the question was studied whether the infection is intensified by placing absorbable sponges into the same pockets.

## EXPERIMENT

The experiments were divided into four groups. In the first group the question was investigated whether sponges alone cause an infection. In the second group sponges and bacteria were implanted together to see whether absorbable material intensifies infection. The third group was concerned with the question whether local application of penicillin is able to suppress the intensification of infection if any by absorbable sponges. In the fourth group the local application of penicillin was replaced by an injection of penicillin at a remote place.

In the first series 4 dogs were anesthetized with subcutaneous morphine injections, followed by intravenous administration of nembutal. The skin on the abdomen was shaved and prepared with iodine followed by alcohol. Four para-rectal incisions, 2 cm. in length and 5 cm. apart were made. The edges were undermined and in each pocket an identical amount, namely 0.3 Gm. of absorbable cotton, fibrin foam,† Gelfoam,‡ or Oxycel respectively was placed. The incisions were closed with interrupted silk sutures. The dogs were killed seven days later and the sites of insertion of sponges were opened under sterile conditions. The gross inspection failed to reveal any signs of infection. Agar cultures after one week incubation period remained negative. The experiments showed that under conditions employed, absorbable sponges alone did not create any infection.

In the second series of experiments 12 dogs were employed using the same technique as in the first series. Through a right para-rectal incision, serving as

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Supplied by Parke, Davis & Company, Detroit, Mich.

†Supplied by Cutter Laboratories, Berkeley, Calif.

‡Supplied by The Wyeth Company, Kalamazoo, Mich.

TABLE I

ROW	CONTROL			COTTON			FIBRIN FOAM			GELFOAM			OXYCEL		
	CULTURE		EXU DATE	CULTURE		EXU DATE	CULTURE		EXU DATE	CULTURE		EXU DATE	CULTURE		EXU DATE
	EXU	TE		EXU	TE		EXU	TE		EXU	TE		EXU	TE	
1															
2															
3															
4															
5															
6															
7															
8															
9															
10															
11															
12															
Total	1	1	0	7	7	6	11	5	7	6	7	5	11	4	8

E = serous P = purulent = positive = negative

a control 0 cc of a virulent staphylococcal culture was implanted into a subcutaneous pocket. On the left side four incision were made the same amount of culture was placed into each pocket and a piece of absorbable cotton fibrin foam, Gelfoam or Oxycel, respectively was inserted. The results recorded in Table I show that of 12 controls, the macroscopic inspection disclosed a serous exudate only in one instance. All the cultures were considered negative because the number of colonies, if any, did not exceed 1 to 3 and this was probably caused by contamination. Of 11 pockets containing absorbable cotton, 3 showed a purulent and 4 a serous exudate. Five cultures had numerous colonies. Of the 11 pockets containing fibrin foam, 9 had a purulent and 2 a serous exudate while 1 had numerous colonies. Of the 12 pocket containing Gelfoam, 1 had a purulent exudate and 4 serous exudates while 7 cultures had numerous colonies. In the 11 Oxycel pockets, there were 2 purulent and 9 serous exudates, with 8 cultures having numerous colonies.

The third series of experiments, employing 10 logs was a repetition of the second series, but after insertion of the sponges, each was moistened with 100,000 units of penicillin. The results (Table II) show that of the 10 control pockets,

TABLE II

ROW	CONTROL		COTTON		FIBRIN FOAM		GELFOAM		OXYCEL	
	EXU	CULTURE	EXU	CULTURE	EXU	CULTURE	EXU	CULTURE	EXU	CULTURE
	DATE	+	DATE	+	DATE	+	DATE	+	DATE	+
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
Total	3	10	0	0	0	0	0	0	0	0



3 contained serous exudates but all cultures were negative. Of the 10 pockets with cotton, 1 had a purulent and 8 a serous exudate and 2 cultures had numerous colonies.

Of the 10 pockets with fibrin foam 9 contained purulent and serous exudates. Five of the cultures contained numerous colonies. Of 10 pockets with G foam, 1 had a purulent and 3 a serous exudate. All cultures were negative. The Oxyeel group had 1 purulent and 4 serous exudates, with 1 positive culture.

In the fourth series of experiment a similar procedure was employed but instead of a local application of penicillin, 300,000 units in oil were administered intramuscularly at a certain distance from the incision. The results are shown in Table III. The control pockets in the 10 dogs contained no exudates and the cultures were negative. Of the 10 pockets with cotton 1 had a purulent and 3 a serous exudate while only 1 culture was positive. Of the 10 pockets with fibrin foam 1 had a purulent exudate and 3 serous exudates, although no cultures were positive. Of 10 pockets with Gelfoam, 2 had serous exudates. All cultures were negative. Of the 10 pockets with Oxyeel, 1 had a purulent and 5 a serous exudate but no cultures were positive.

TABLE III

DOG	CONTROL		COTTON		FIBRIN FOAM		GELFOAM		OXYEEL	
	EX DATE	CULTURE	EX DATE	CULTURE	EX DATE	CULTURE	EX DATE	CULTURE	EX DATE	CULTURE
1		x							h	x
2		x								x
3			H		H		H		H	
4		x	H		H		H		H	
5			H		I				h	x
6				x					h	
7				x						
8		x	P						P	
9				x						
10					H					
Total	10	0	4	9	1	1	10	0	1	10

## COMMENTS

The experiments showed that absorbable sponges have a tendency to intensify an infection created in subcutaneous tissues of dogs by *Staphylococcus aureus*. This tendency was slightly more pronounced in certain brands of absorbable sponges than in others. Mortening of the absorbable material with penicillin did not inhibit the effect which, however, could be eliminated by concurrent administration of penicillin in oil intramuscularly. Only *Staphylococcus aureus* was employed in the experiment. It is realized that infections caused by other pathogenic microorganisms may not be intensified by absorbable sponges.

As far as abdominal surgery is concerned, this undesirable effect of absorbable sponges may be of no practical importance in infections of the abdominal cavity. The results of the present experiment suggest the true value of absorbable sponges in the treatment of abdominal infections.

employed in presence of an infection, or in cases where the development of an infection during the postoperative period is feared. It is probable that an aqueous solution of penicillin would be just as effective as penicillin in-oil in the inhibition of infection, but since we used penicillin in-oil (thus eliminating frequent injections) our conclusion is based on that type of administration.

#### SUMMARY

1 Experiments on dogs showed various brand of absorbable sponges to have a tendency to intensify infection created in subcutaneous tissues by *Staph aureus*.

Moistening of absorbable sponges with penicillin was not able to prevent this effect.

3 Intramuscular administration of penicillin in-oil inhibited the intensification of infection caused by absorbable sponges.

4 Administration of penicillin in-oil is recommended whenever absorbable sponges are employed in presence of a manifest or anticipated infection.

We wish to express our gratitude to Dr. Warren H. Cole for his valuable suggestions and the privilege of performing the experiments in the laboratory of the Department of Surgery, University of Illinois College of Medicine.

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## COMPLICATIONS OF IMPERFORATE ANUS REPAIR

FURMAN T. WALLACE, M.D. AND F. M. COLVIN, M.D. SPARTANBURG, S. C.

(From the Department of Surgery, Spartanburg General Hospital)

IMPERFORATE anus repair has advanced so that in most instances the entire procedure is done from the perineal approach. X-ray localization of the blind pouch, taken with the child in an inverted position (Fig. 1) has particularly stimulated primary repair. A preliminary colostomy is practically never necessary. When extensive dissection is required in the newborn infant, particularly in instances where the blind end of the colon is high, technical complications are likely to occur.

### URINARY TRACT INJURIES

In the male infant the urethra and bladder are especially endangered. In one instance the urethra was snapped at the junction with the bladder the prostate remaining in place.

*Prophylaxis*—A small urethral catheter should be passed into the bladder and anchored to the prepuce with a suture. This serves as a guide by palpation, and also by visualization if the thin urethra is approached closely or actually entered.

Also, the urethra is splinted by the catheter and is less likely to be torn by traction on the surrounding structures. This is important at the urethrov vesical junction, because the prostatic urethra is fixed by strong fascia, and the bladder can be pulled away from it.

*Repair*—A small laceration of the urethra would require only the indwelling catheter for about ten days.

In the instances where the bladder was pulled away from the prostatic urethra no catheter had been anchored preoperatively. The internal urethral orifice was seen as a small aperture in the bladder no urethra being attached. The distal end, or prostatic urethra, was not visible through the incision.

A catheter was passed through the penis and became visible from behind the symphysis pubis. The catheter was passed into the bladder through the aperture (internal urethral orifice) and anchored with a single suture.

The catheter was withdrawn from the penis to the limit of gentle traction and anchored to the glands with a suture (Fig. 2). This replaced the bladder and urethra in their proper relationship. Healing occurred without early or late complications.

### SEPARATION OF ANAL SUTURE LINE

The anastomosis of the mucosa to the anal skin should hold and primary union take place. When the blind end is unusually high partial or complete separation sometimes occurs.

*Prophylaxis*—The essential factor in primary union is the absence of tension on the suture line. The pouch must be mobilized freely so that it falls into position against the anal skin.



Fig 1—X-ray taken in inverted position end of blind pouch seen as shadow  
sacral segment, marker I small position of anus

third

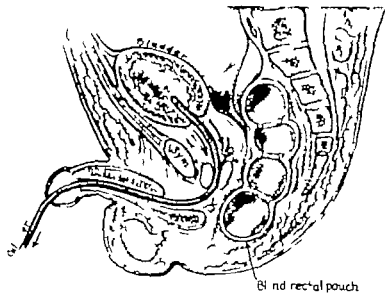


Fig 2—Displacement of bladder by traction on catheter anchored to bladder neck

The wall of the bowel must be preserved by gentle handling. It is particularly difficult to compensate for any defects resulting from tearing by undue traction.

**Repair**—When part of the circumference of the anastomosis separates, a stricture results. Postoperatively frequent dilations are necessary for a considerable period. These patients must be followed closely and dilatation done

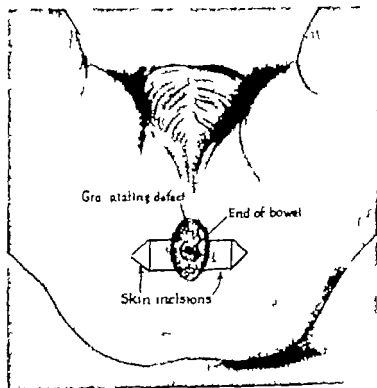


Fig. 3—Incisions for pedicle graft. The rectangular area forms the skin tube, the triangular areas are excised to permit tension-free closure.

with the gloved finger at least once a week for several months. At the early dilations there will be some tearing of the stricture with bleeding. The lumen gradually enlarges, probably due to growth of the mucosa over the raw surface for a small distance each time the stricture is dilated. At about the age of 6 months the lumen remains large and frequent dilations are no longer necessary. There should be a checkup at regular intervals to guard against recurrence of the stricture.

If the anastomosis separates completely a plastic pedicle form skin-lined anal canal may be necessary. This may be done before healing of the resulting defect begins. A ring of mucosa in the depths of a trough lined by granulation tissue is seen as the separation causes the skin edges to retract so that the

The separation causes the skin edges to retract so that the

At the secondary operation an incision outlining a rectangular area of skin is made on each side (Fig 3). This incision is carried down to mobilize this area from the surrounding skin but is left attached on its deep surface to the subcutaneous tissue. A rectangular area of skin thus rests on a pedestal of subcutaneous tissue. This pedestal graft is freely movable in all directions and can be placed against mucosa of the bowel without traction (Fig 4). The resulting defect in the gluteal area is closed holding the pedestal grafts on each

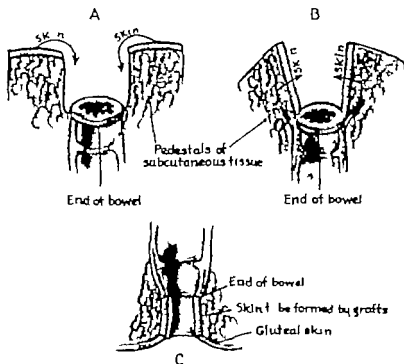


Fig 4—A. Pedestal graft prepared. B. pedestal grafts, forming skin tube. C. end result.

side in position. Suture of the skin to the mucosa is necessary. The grafts are not sutured to each other but fall into position as healing of the defect anteriorly and posteriorly occurs, forming a skin lined tube. The outer portion of the grafts are anchored to the skin margins.

A careful postoperative dilatation regime is essential to prevent the deep end of the skin tube from growing together and to create a structure for maturation at the junction of skin tube and mucosa.

#### SUMMARY

Certain complications of imperforate anus repair are presented and method of prophylaxis and treatment are suggested. The use of pedestal grafts is introduced.

The wall of the bowel must be preserved by gentle handling. It is particularly difficult to compensate for any defects resulting from tearing by undue traction.

*Repair*—When part of the circumference of the anastomosis separates, a stricture results. Postoperatively frequent dilations are necessary for a considerable period. These patients must be followed closely and dilatation done

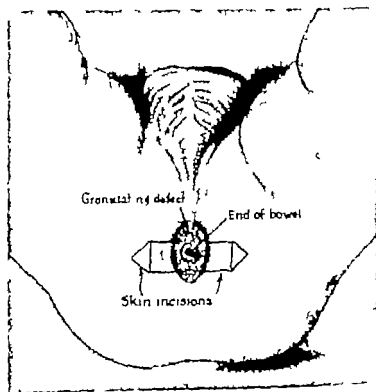


Fig. 2.—Incisions for pedicle graft. the rectangular area forms the skin tube, the circular areas are excised to permit tension on closure.

with the gloved finger at least once a week for several months. At the early dilations there will be some tearing of the stricture with bleeding. The lumen gradually enlarges, probably due to growth of the mucosa over the raw surface for a small distance each time the stricture is dilated. At about the age of 6 months the lumen remains large and frequent dilations are no longer necessary. There should be a checkup at regular intervals of several years to guard against recurrence of the stricture.

If the anastomosis separates completely a plastic covered rectum and lined anal canal may be necessary. This may be done before healing of the resulting defect begins. The bowel is seen as a ring of mucosa in the depth of a trough lined by granulation tissue. The separation causes the skin edges to retract so that the gluteal crease is obliterated.

sequestra of cartilage present. All diseased artilage was removed down to bleeding bone except for a circular area about 1 cm. in diameter in the center of the diseased area in which the bone was so dense and elaborated that it did not bleed even when drilled quite deeply. No other abnormality was found.

The cyst consisted of one large and one small loculus which did not communicate with each other. It contained thick, gelatinous material. Microscopic examination revealed typical ganglion structure with the wall formed of concentric layers of flat celled fibrous tissue and no true endothelial lining (Figs 1 to 3).

The postoperative course was uneventful. Quadriceps setting exercises were begun twenty-four hours after surgery. Sutures were removed on the tenth day and weight-bearing was begun on the twelfth day. Full range of motion was regained in twenty days. The patient was able to return asymptomatic free to employment as a clerk after thirty days.

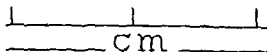


Fig. 1.—Anterior surface of cyst. Fibers of the anterior cruciate ligament can be seen above the cyst. Parallel marks at the lower edge were caused by the forceps with which the cyst was grasped during operation.

While at first glance this cyst projecting into the intercondylar notch appeared to be intra-articular and so did not meet the criteria for a ganglion, its origin from the anterior cruciate ligament made it the characteristic extra-articular lesion albeit in an unusual location. It is this unusual aspect of the case which may serve to shed some light on the prevailing theories of the etiology of ganglia. These theories have been discussed by several authors. Those given the widest credence today are

- 1 Metaplasia of specialized periarthral connective tissue so that it develops a secretory action forming a pseudojoint cavity (King)



# A GANGLION OF THE ANTERIOR CRUCIATE LIGAMENT

JACK LEVINE M.D. BRONX, N. Y.

(From the Orthopedic Section Veterans Administration Hospital)

ALTHOUGH ganglia are found with relative frequency in the peritendicular tissues of the knee, the presence of a ganglion on a cruciate ligament is very uncommon. A review of the literature has revealed only two cases in which the formation of a ganglion on a cruciate ligament has been noted.<sup>1,2</sup> The following case is, therefore, reported because of its rarity and because it appears to be the first of its kind to be described in the English literature.

## CASE REPORT

The patient, 23 years old, hit man (Reg. No. 93433) was admitted to the Orthopedic Section of the Kingsbridge Veterans Administration Hospital on May 31, 1947, with the complaint of pain and recurrent attacks of pain in the left knee for three years. In September 1944, he had fallen into shell hole at night while in combat in Italy and twisted the left knee. He had immediate pain and swelling which required his evacuation to hospital where he was placed in a long leg plaster for three weeks. He was then given physiotherapy for three more weeks and at the end of that period was well enough to return to duty. Thereafter he had only occasional attacks of relatively mild pain and swelling until January 1947 when the left knee suddenly locked while he was walking on even pavement. This occurred about once monthly from then until May 12, 1947, when, while playing baseball, the knee gave way again as he made a sudden turn. While the knee did not lock, he was unable to extend it fully for about thirty minutes because of severe pain, but at the end of that time he was able to straighten the knee and walk. Swelling occurred within ten hours. He stayed at home for the following week under the care of a physician, but when he failed to respond to conservative therapy he was admitted to the hospital for further treatment.

Physical examination on admission revealed that the patient walked with a limp on the left leg. There was one inch trophy of the left thigh with corresponding diminution of tone in the left quadriceps. There was moderate swelling of fluid in the left knee. Range of motion was complete but there was some pain referred to the medial aspect of the knee joint on full flexion. On relaxation of the collateral or cruciate ligaments was found. There was tenderness to pressure over the anteromedial aspect of the knee joint.

X-ray findings, including lateral view and tangential view of the patella, were negative. Urinalysis, blood count, serology and sedimentation rate were not remarkable.

Although osteoarthritis distal to the patella appeared likely as definite diagnosis was established preoperatively. An exploration of the knee seemed advisable. On May 29,

ending 1947

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- \* Synovial rests in the developing periarticular connective tissue later form ganglia (Harrison)
- 3 Herniation of the synovial lining of a tendon sheath or joint capsule (Eller Doyle)
- 4 Myxomatous degeneration of specialized periarticular connective tissue forming a pseudocyst (Lacklerhose)

Doubt has been cast before on the accuracy of King's theory since by the use of Mayer's mucinamin stain it has been shown that the contents of ganglia are myxoid and thus due to a degenerative process rather than mucinous and a true secretion. The same argument would hold against Harrison's theory.

In our case at least it seems unlikely that herniation of the synovial lining occurred. The density and length of the anterior cruciate ligament make it unlikely that this would happen. It seems more likely that the ganglion formed in a local area of degeneration. Whether this was due to a congenital abnormality of the ligament or to the trauma which he suffered cannot be definitely ascertained. However the fact that most ganglia form in other locations, with no definite history of trauma makes it appear unlikely that injury was an important factor.

We could establish a definite causal relationship between the existence of the ganglion of the anterior cruciate ligament and the osteochondritis of the patella, unless the abnormal mechanics of the knee extension apparatus due to the osteochondritis precipitated degenerative changes in the anterior cruciate ligament. In this event our hypothesis would still hold true.

The symptoms of a ganglion of a cruciate ligament do not appear to be constant. The limited experience with this entity has revealed a wide range of complaint in the ten previously reported cases from no symptoms at all to severe disability.

In 1941 (an unpublished case) which was completely asymptomatic. The ganglion was an incidental finding in the knee of a cadaver which was being subjected to a knee resection during a course in cadaver surgery. A review of the patient's medical history revealed no complaint referable to the knee. The pathological findings consisted of a hazelnut-sized unilocular ganglion in the middle of the anterior cruciate ligament completely covered by dense fibers except in one small area where the external wall projected beyond the fibers. In addition, two smaller ganglia comprised separate from the first, were found within the anterior cruciate ligament. None was found anywhere else in the body.

Spivack's case reported in 1941, was that of a 31-year-old woman who, ten years prior to hospitalization had had an episode of unexplained effusion in the left knee. There was no preceding trauma, illness and the only symptom at that time was tension in the knee. It disappeared after three weeks of bed rest. She remained symptom free until several years later when she jumped during a game of volleyball and while in the air felt severe pain in the left knee. The knee did not lock but there was severe pain along the medial aspect of the joint line and a effusion soon developed. After three weeks the effusion subsided.

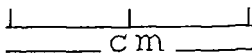


Fig. 2.—Inner surface of cm. dense fibers of interior crucia. (Mounts are all stained.)



Fig. 3.—Section of cm. (148) shows characteristic sargasso formation. Note lack of true endothelial lining.

# CONGENITAL ATRESIA OF THE ESOPHAGUS WITH HYPOPLASIA OR AGENESIS OF THE LOWER SEGMENT

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(From the Department of Surgery, University of Michigan Hospital, Ann Arbor, Mich.)

CONGENITAL atresia of the esophagus is now recognized as a common anomaly. The relative incidence of this congenital defect has been discussed by Haight,<sup>1</sup> and by Ladd and Swenson. Haight estimated that the anomaly occurs once in each 4,196 births. The diagnosis, if the clinician is alert to the possibility of its presence is easy. The observation that the infant is unable to swallow, that it regurgitates immediately all fluid offered, and that choking, dyspnea and cyanosis occur should make the diagnosis probable. Confirmation of the diagnosis is obtained when a soft rubber catheter (8 or 10 French) fails to pass into the stomach.

A few drops of lipiodol injected into the catheter will either delineate the upper segment as a blind pouch (the common finding), demonstrate a fistulous communication between the upper segment and the trachea (a rare anomaly) or indicate that esophageal continuity through a striated area is present (a still rarer type of defect).

In addition to demonstrating the presence or absence of atelectasis or pneumonia, the x-ray film will reveal the presence or absence of air in the stomach or intestine. It is with the cases of atresia, in which no air is visible in the stomach, that this discussion is concerned. When air is present it indicates that a tracheoesophageal fistula is present, that the lower segment of the esophagus is patent, and that it extends as high as the tracheal bifurcation. (Haight reported a case in which the fistulous communication was between the esophagus and the right main stem bronchus.) These patients may therefore be considered as suitable candidates for a right-sided extrapleural division of the fistula and a primary esophageal anastomosis, the accumulating experience of many authors demonstrating this operation to be the procedure of choice.

The absence of air in the stomach does not necessarily mean that a tracheoesophageal fistula is not present nor that primary anastomosis is not feasible. Haight reported that five patients without air in the stomach had a small but patent fistula. Four of these patients were subjected to operation and in one primary anastomosis was possible. In a subsequent paper to be published he reports that ten of sixty-two patients with esophageal atresia had no air in the stomach. Of these seven were subjected to operation. Anastomosis of the esophageal segments was possible in two, but the approximation of the segments was not satisfactory. In five anastomosis was not possible. For this reason, tracheoscopic examination is indicated. If this procedure also fails to demonstrate the presence of a fistula the patient should be considered unsuitable for the right-sided extrapleural approach. A decision must then be made as to whether to employ the multiple stage operation which consists of marsupialization of the superior segment, gastrostomy and eventual construction of an antithoracic esophagus to try to bring about direct esophagogastric continuity.

sided but the pain persisted in the same place. She had to give up all forms of athletics and even walking caused some pain. Four years later when she was finally hospitalized there was no effusion noted but there was some quadriceps atrophy and definite genu recurvatum. There was point tenderness over the anteromedial aspect of the knee joint. X-ray findings were negative. At operation a multilocular ganglion, about the size of two beans, was found arising from the posterior cruciate ligament at the point where it was partially detached from the tibia. The ganglion was removed but no attempt at repair of the ligament was made because most of the fibers were intact. The postoperative course of the case was not discussed in this paper.

Sjovall felt that the ganglion had antedated the onset of symptoms and probably weakened the posterior cruciate ligament sufficiently to cause a partial rupture of it when the knee was exposed to relatively mild trauma.

In our case the role played by the ganglion in the causation of symptoms was so clouded by the presence of the extensive osteochondritis of the patella that any attempt to form definite conclusions would seem unjustified. The latter finding alone could have caused all the complaints. However at the time of operation, it was deemed advisable to remove the ganglion. We felt that it might eventually have involved more of the anterior cruciate ligament, weakening it sufficiently to cause disability or that it might grow large enough to obstruct the movements of the knee.

#### SUMMARY

A case has been presented in which a ganglion of the anterior cruciate ligament and osteochondritis of the patella were found. The ganglion was probably formed in a localized area of degeneration in the anterior cruciate ligament. None of the symptoms could be attributed definitely to the ganglion but it was removed because it was potentially harmful. This appears to be the third case of a ganglion of a cruciate ligament to be described.

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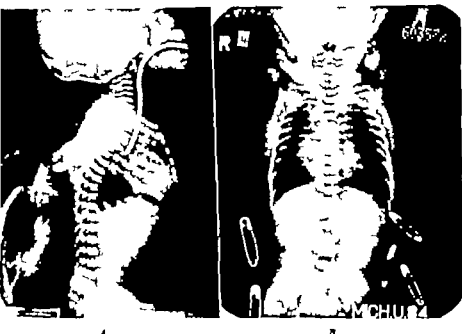


FIG 1 (Case D H). —A X-ray was taken the day prior to admission showing the catheter in the blind upper esophageal pouch. B The posteroanterior film taken on the day of admission reveals the prominence of the right ventricle and the continued presence of air in the stomach.

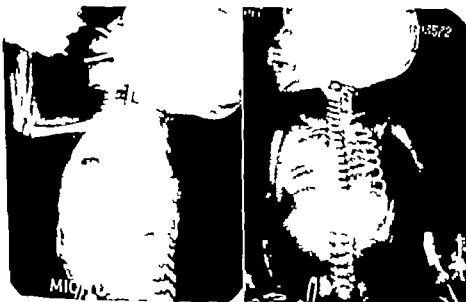


FIG 2 (Case D H). —A Horizontal exposure, taken the day following operation, demonstrates the intrathoracic stomach. B Oblique view on the fifth postoperative day outlines the position of the air-filled stomach.

The disadvantages of the multiple stage operation are obvious, a prolonged period of hospitalization and numerous operations being required. Ladd and Swenson have used this method in forty three patients, sixteen of whom survived. Of these sixteen patients, completion of the antebornack esophagus has been obtained in but five at the time of their report.

An attempt to establish direct esophagogastrostomy by mobilizing the stomach and anastomosing it to the blind upper segment above the aortic arch had not been made to my knowledge, prior to its use in the case here described. Subsequently Swenson reported a case in which this procedure was successfully employed.

#### CASE REPORT

D. B. male, birth, aged 4 days, was admitted to the University of Michigan Hospital on April 29 1947. He had been delivered spontaneously five and one-half months premature. Birth weight was 5 pounds, 10 ounces. He was put to breast twelve hours after birth, but because cyanotic gagged, hiccups and obviously unable to swallow. Several feedings were attempted. A small catheter was then inserted into the esophagus and found to pass for only 10 cm from the lips. An x-ray view confirmed the presence of obstruction revealed that the lung fields were clear and that there was no air in the stomach. A diagnosis of stenosis of the esophagus was made and he was referred for surgical treatment.

The physical examination on admission, revealed that he cried loudly becoming cyanotic. Cyanosis was not present, however during normal respiration. The lung fields were clear to percussion and auscultation, and no heart murmurs were audible. There was no abdominal distention. His state of hydration was good as he had received colostrum plus cow colostrum prior to admission. An x-ray picture obtained at the University of Michigan Hospital revealed the continued absence of air in the stomach or intestines, normal lung fields, and pericardial triangular prominence of the right heart border the significance of which was not clearly understood.

Because of the absence of air in the stomach, it was felt that marked hypoplasia or aganglionosis of the lower esophageal segment was present. Therefore retropharyngeal anastomosis did not appear to be feasible and left thoracotomy was decided upon. Operation was carried out under ether anesthesia on the day of admission. The ether was administered by open drop, right flung face mask being used to give oxygen under positive pressure after opening the pleural cavity. Access to the chest was through the bed of the resected seventh rib. An excellent exposure was obtained without further dissection of ribs.

By blunt dissection the pleural cavity was opened and the lung was found to be normal.

The aortic arch was communicated directly between it and the trachea. The inferior vena cava as then mobilized by separating the leaves of the pulmonary ligament. It was found that the caliber was normal for only 1.5 cm. below the aortic arch. At this point it narrowed sharply to a threadlike cord and at the level of the inferior pulmonary vein was merely a thread. This threadlike strand continued downward beneath the aortic arch and was found to be attached to the membranous portion of the left main stem bronchus.

The diaphragm was then opened from below the anterolateral costal attachment. The stomach as found to be very small. The first step in the mobilization of the stomach consisted in the division of the gastrophrenic ligament close to the spleen as possible. The spleen was not removed and subsequently did not interfere with the mobilization. The gastrohepatic ligament was then divided the left gastric artery being ligated close to its origin. When this procedure was completed the fundus of the stomach could easily be drawn to the level of the aortic arch with only slight tension. The lower segment of the esophagus was then amputated and closed by through and through sutures which was continued back upon itself as a seromuscular suture. A row of 000000 black silk sutures was then placed between the blind esophageal end and the fundus of the stomach. The end of the esophagus

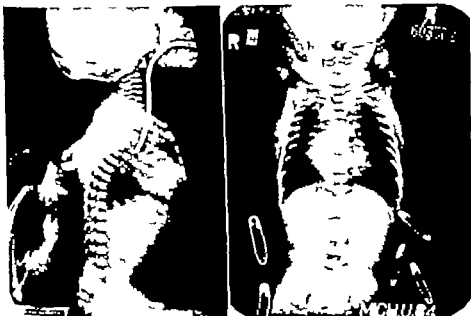


Fig 1 (Case D B) — A X-ray was taken the day prior to admission showing the atresia in the blind upper esophageal pouch. B The posterior (erior film taken on the day of admission reveals the prominence of the right ventricle and the continued presence of air in the stomach.

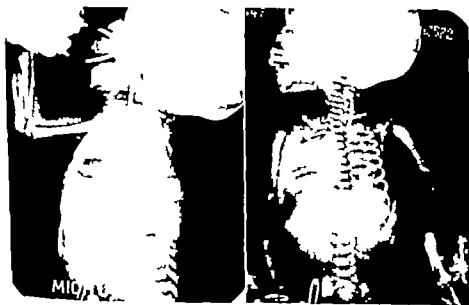


Fig 2 (Case I H) — Kymograph taken the day following operation demonstrating the intrathoracic stomach. B Oblique view on the fifth postoperative day certifies the position of the air-filled stomach.



as then opened, creating 1 cm stoma, and a similar incision was made in the fundus. The muscular layers were then approximated posteriorly and anteriorly by interrupted No. 000000 silk sutures. A second anterior row of similar sutures approximated the muscular layers of the esophagus to the seromuscular layers of the stomach. A No. 16 French soft rubber catheter was then passed from above into the stomach. The stomach was fixed to the pleura overlying the vertebral bodies. The diaphragm was then closed but not sutured to the pyloric end of the stomach. The pyloric hole was crushed. A small soft rubber catheter was employed as an intercostal drainage tube and carried to the water seal bottle. Penicillin, 100,000 units, was instilled into the pleural cavity and the chest closed with interrupted silk sutures. There was very little blood loss during the procedure, but since the extra cardiac circulation had ceased to function after only 10 c.c. of blood had been given, intra cardiac injection of 20 c.c. of blood was performed midway during the operation.



Fig. 3 (Case D B). Anterior specimen showing the rib-headed line of anastomosis. (A) the edge of the aorta; (B) the edge of the aorta; (C) the edge of the diaphragm.

Postoperatively penicillin, subcutaneous glucose (25 per cent) and small transfusions were given. Intercostal drainage was discontinued after seventy-two hours. The catheter was removed from the stomach after forty-eight hours. Fluids by mouth were withheld for forty-eight hours and then a few drops of 5 per cent glucose-saline solution were given cautiously by dropper. He appeared to be able to swallow but immediately became cyanotic. About 10 c.c. of similar solution were given by gavage feeding and this was apparently well received. However subsequent passage of the catheter accomplished with ease, caused the baby to cry. With each attack of crying he became extremely cyanotic and with unpleasant stimuli, such as the introduction of the stomach tube or the injection of penicillin, respiratory arrest would ensue so that artificial respiration and CO-O<sub>2</sub> inhalations were required. On the eighth postoperative day crying attack with cyanosis and cessation of respiration occurred and the nurse was unable to revive him.

At autopsy the left pleural cavity contained only 1 cm. blood clot, the lung was expanded, and the base of extracardiac anastomosis was rib-headed, the stoma measuring 1 cm. in diameter. The myocardium of the right ventricle was greatly hypertrophied, and was 2 mm. thicker than that of the left ventricle. What at first inspection seemed to be a double aortic arch proved to be ductus arteriosus as large as the aorta itself. There was hypoplasia of the right and left pulmonary arteries, the ductus arteriosus being direct recipient

best of the main pulmonary artery. It is apparent that the chief flow of blood from the right ventricle passed directly into the aorta.

It was evident from the autopsy findings that the peculiar cardiac silhouette was due to the greatly hypertrophied right ventricle. A cardiac murmur had not been present because of the large size of the ductus arteriosus and for the same reason a palpable aortic thrill was not present at operation.

Although this child succumbed as a result of the operation, the cardiovascular anomalies being the indirect cause of death, the case does illustrate that these infants do tolerate major intrapleural surgery and that direct esophagogastronomy is not only feasible but can be accomplished with ease.

A few points in the operative technique seem worthy of mention. Since the gastrosplenic ligament is extremely short, the vasa brevia measuring only 2 to 4 mm in length care must be taken to divide it close to the spleen in order to preserve the anastomotic vessels along the greater curvature of the stomach. As the upper esophageal segment ends in a blind pouch the size of the stoma of the anastomosis is not dependent upon the caliber of the upper segment since a full-mouth incision can be made to create a stoma of any desired size. A three-layer anastomosis can be utilized but add to the technical difficulties and the operative time, and it does not appear to be necessary. As with esophagogastronomy in adults, resection of the seventh rib gives good exposure of the abdomen and the region of the aortic arch, thoracoabdominal incision and multiple rib resection not being required. The intra-aortic injection of whole blood, oxygenated if desired, is a positive method of maintaining blood volume.

The failure to employ tracheoscopy as a preoperative diagnostic measure in this case was a serious omission. Although the anatomic findings in this case precluded any chance of extrapleural primary anastomosis, this possibility had not been completely ruled out before operation.

#### SUMMARY

In patients with congenital atresia of the esophagus in whom the x-ray examination fails to reveal evidence of air in the stomach or intestine, marked hypoplasia or agenesis of the lower segment may be inferred. An adequate lower segment may however be present in a small percentage of cases.

When there is failure to demonstrate air in the stomach and a tracheoscopy discloses no tracheoesophageal fistula, an extrapleural exploration seems futile and a left transpleural esophagogastronomy is indicated.

The operation of high esophagogastronomy in newborn infant is feasible and the operation itself was well tolerated in the case here presented. Although the infant died death appeared to be due largely or entirely to the associated cardiovascular anomaly.

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# STRANGULATING DIAPHRAGMATIC HERNIA OF THE LIVER

## REPORT OF CASE WITH SURGICAL CURE

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DIAPHRAGMATIC hernia is not uncommon; its classification, symptomatology, diagnosis, and treatment have been sufficiently reported.<sup>1</sup> Hernia of the right side is unusual compared with the left; the ratio is reported as 1 to 1 (Bradley) and 1 to 1 (Hedblom). Hernia containing only a mass of liver is rare; thus the liver alone was found in only 14 out of 857 cases of diaphragmatic hernia.

Operation was performed with resulting cure upon a patient who had both herniation of a portion of the liver through the diaphragm, and strangulation of this liver. Detailed reports of congenital hepatic herniation treated surgically are rare and we have not been able to discover even one report mentioning strangulation of the liver. The bizarre symptom ascribed to this hernia and its strangulation have not to our knowledge been previously reported.

### CASE REPORT

A 47-year-old white housewife came for the first time Aug. 4, 1948, with chief complaint of attacks of epigastric pain, nausea, and vomiting of a monthly duration.

The family history revealed that the mother had died at the age of 83 years, and the father at the age of 67 both of cardiac disease but specific character undetermined. Five sisters died—cause of unknown causes and three sisters are living and well. There were no brothers and no contact with tuberculosis.

The past history showed diphtheria in childhood with no sequelae; there were no other childhood diseases. There had been no previous operations or accident. The patient had been married twice and had had no pregnancies. Birth history unremarkable and no knowledge of any abnormalities. There was no history of chronic cough, repeated physical strain, or any other condition that could cause increased intra-abdominal pressure.

A review of the systems showed nervous breakdown in 1925 with symptoms of anxiety neurosis, and irritability but without gastrointestinal manifestations, and leading to a month's absence from work. There had been no complaints in striking the head, neck, eyes, nose, or throat. The cardiorespiratory history revealed the knowledge of numerous acute attacks but no episodes of dyspnea, cyanosis, orthopnea, hemoptysis, paroxysmal pleurisy, or other cardiorespiratory complaint. The gastrointestinal history until the present illness, as well as for dyspepsia, food intolerance, constipation or hemorrhoids. The gynecological history was unremarkable. Venereal disease was denied by signs, symptoms, and tests. Catamenia 17 to 5 by 27, then dysmenorrhea and with last menstrual period, July 24, 1948. She did not use tobacco or drugs, and the only alcohol was socially. Weight had been maintained at about 147 pounds with very little fluctuation.

During the time of admission the chief complaints had begun six months previously in attacks occurring on an average of once a month. The attack consisted of epigastric pain, nausea, and vomiting. The onset of the pain was gradual over a period of about five minutes, after which it reached its maximum intensity, remained constant for three to eight

liver was centered in spot just beneath the xyphoid and described as squeezing, heavy and ball-like, its cloudlike spreading to both sides but not to the back, to the shoulders, under the sternum, or to the scapular areas and vomiting began when the pain reached maximum intensity and frequent throughout the attack. There was no associated diarrhea or constipation. The attacks extended spontaneously but could be terminated by an injection of .4 gr of morphine sulfate. She felt sick for one or two days following the attack but was otherwise in perfect health. She stored the information that at all times between attacks she had feeling like doorstop in the lower right chest, back bending motion on bending forward and the right



Fig. 1

Fig. 2

Fig. 1—Anteroposterior roentgenogram of the chest, postmanipulation. The lungs are generally clear, rounded mass is visible in the right phrenopericardial sulcus. Note the appearance of discrete tumor in the displaced anterior view.

Fig. 2—Anteroposterior roentgenogram of the chest, high lateral view, postmanipulation. The mass is visible in the right phrenopericardial sulcus, just anterior to the tenth dorsal vertebra, not displacing the esophagus.

During the first attack on August 4, 1946, the temperature, pulse and respirations were normal. The patient was in obvious distressing pain. The pupils were regular and reacted to light and accommodation. The fundi were normal. There was no change in the left temperature. The tongue for the lower mouth and pharynx were normal. The throat was normal at the trachea and in the larynx. There were no abnormal cervical vessels or pulsations. The lungs were clear. There was no pleural effusion. The right enlargement of the lungs was of good quality. There was moderate loss and rough, vital signs. The third intercostal space just to the left of the sternum was not examined in any direction. There was no thrill palpable. The blood pressure was 110 systolic and 60 diastolic. There was mild tenderness tenderness in the sixth dorsal vertebra. The breasts were normal. The abdomen was soft and revealed no abnormality except for mild tenderness high in the epigastrium and deep pressure. The abdominal examination was essentially normal. The extremities were normal and there was no swelling. There were no hernias or edema. The mucous membranes were pink. Four hours later the patient was taken to the hospital with one half hour by an injection of .4 gr morphine sulfate.

# STRANGULATING DIAPHRAGMATIC HERNIA OF THE LIVER

## REPORT OF CASE WITH SURGICAL CURE

SAMUEL A. WOLFSON M.D. AND ALFRED GOLDMAN M.D. LOS ANGELES, CALIF.

(From the Thoracic Surgical and Medical Services of the Cedars of Lebanon Hospital)

DIAPHRAGMATIC hernia is not uncommon; its classification, symptomatology, diagnosis, and treatment have been sufficiently reported.<sup>1-4</sup> Hernia of the right side is unusual compared with the left; the ratio is reported as 12 to 1 (Bradley)<sup>5</sup> and 7 to 1 (Hedblom).<sup>6</sup> Hernia containing only a mass of liver is rare; thus, the liver alone was found in only 14 out of 837 cases of diaphragmatic hernia.

Operation was performed with resulting cure upon a patient who had both herniation of a portion of the liver through the diaphragm, and strangulation of this liver. Detailed report of congenital hepatic herniation treated surgically are rare and we have not been able to discover even one report mentioning strangulation of the liver. The bizarre symptoms ascribed to this hernia and its strangulation have not to our knowledge, been previously reported.

### CASE REPORT

A 47-year-old, hit woman of Jewish descent for the first time Aug. 4, 1916, with chief complaint of attacks of epigastric pain, nausea, and vomiting of six months duration.

The family history revealed that the mother had died at the age of 8 years, and the father at the age of 63 both of cardiac disease but specific character undetermined. Five sisters died in infancy of unknown causes and three sisters are living and well. There are no brothers and no contact with tuberculosis.

The past history showed diphtheria in childhood with no sequelae. There were no other childhood diseases. There had been no previous operations or accidents. The patient had been married twice and had had no pregnancies. Birth history contained no knowledge of any abnormalities. There was no history of chronic cough, repeated physical strain, or any other condition that could have increased intra-abdominal pressure.

A review of the symptoms showed nervous breakdown in 1912 with symptoms of anxiety, nervousness, and irritability but without gastroenteric manifestations, and lasting six months. Recovery was complete. There had been no complaints involving the head, ears, eyes, nose and throat. The cardiovascular history revealed the knowledge of a murmur since infancy but no episodes of dyspnea, cyanosis, orthopnea, hemoptysis, peripheral phlebotomy or other cardiovascular symptoms. The patient was negative for dyspepsia, of gastrointestinal history as essentially negative and name. Catamenia 1 by 3 by 7, normal.

Illness began with attacks occurring on the first stage of onset. The attack consisted of epigastric pain, nausea, and vomiting. The onset of the pain was gradual over a period of about five minutes, after which it reached its maximum intensity remained constant for three to eight

posterior bed of the seventh rib. A globular mass bulged (Fig. 3) through the posterior medial leaf of the diaphragm at the pleural cavity for distance of  $\frac{1}{4}$  inches. The bulge was very firm and had impressed itself into the diaphragmatic surface of the right lower lobe. The surface of the tumor as thickened by adhesions which were continuous with the inferior pulmonary ligament, the right diaphragmatic crura, and the base of the right lower lobe. The neck of the herniating pleural mass was constricted about 50 per cent as it traversed the ring of tendinous diaphragm. Posterior and medial to the mass as the deflected inferior vena cava.

There was a well-defined, vesicular, mesentery-like transparent cil, approximately 5 inches in length, with its superior border attached to the visceral pleura—an arc beginning laterally about 4 inches above the diaphragm at the posterior axillary line and extending medially to attach on broad base on the diaphragm and continuing around the mass to the inferior vena cava. This veil was incised in order to approach the tumor. When the mass was separated from adherent lung and diaphragm the bulge as found to be covered by thinned out tendinous diaphragm and Glisson's capsule. The tendinous, constricting defect in the diaphragm produced a broad, pedicle-like appearance to the herniated, strangulated liver. This mass was bisected, and frozen sections showed it to be normal liver.



Fig. 3.—Feb. 4, 1911. Anterior view of the chest six months after surgical repair of the strangulated diaphragmatic hernia of the liver. Six months after removal of the seventh rib, the high diaphragm due to phrenic nerve crush and the absence of an tumor mass. The patient has been free from attacks since operation.

The tendinous, diaphragmatic constriction was incised in order to reduce the strangulated liver and allow it to drop below the diaphragm. At this time the subdiaphragmatic space was explored and no other pathology was found. A few minutes later, but had been to each sphere had now shrunken to almost the configuration of normal dome of the liver as though it had been accommodated into the li itself. The diaphragmatic hernia was repaired by suturing the phrenic nerve as crushed to the diaphragm in layers with interrupted sutures. The end of the whole blood.

Diaphragmatic hernia as suspected and the patient as hospitalized for observation and investigation at the Ordway of Lebanon Hospital on Aug. 11, 1946.

While undergoing investigation the patient remained asymptomatic. The physical examination was as just described, with the deep epigastric tenderness absent. The erythrocyte count, hemoglobin, white blood cell count and differential count were normal. The red cell morphology and platelet were normal. The sedimentation rate was 1 mm. in 144 minutes (Westergren—normal, 1 mm. 120 minutes). Blood alcohol red as 240 mg per cent. The acetone index was 7 units (normal, 8 to 12 units). The urine was normal and showed no bile. The blood Kline reaction was negative.

Fluoroscopic examination and x ray view of the chest (Figs. 1 and 2) showed sharply defined, nonpalpating, globular mass thought to be in the posterior portion of the right mediastinum, just below the dome of the right diaphragm, but apparently not moving with respiration, although the diaphragm thought to move freely. The mass measured about 7 cm. in diameter and had no apparent connection with mediastinal structures. Oral cholecystography showed normally functioning gall bladder without stones. A barium swallow was

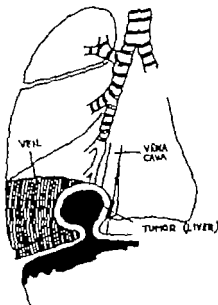


FIG. 2.—Fluoroscopic picture of certain findings with the contrasted back of the liver and not stratified liver (the diaphragm).

negative. Gastrointestinal study showed the esophagus, stomach, and duodenum to be free of abnormalities. The spherical tumor mass in the right lower mediastinum, as well separated from the cardiac portion of the stomach, ruled out hiatus hernia. However, no metastatic lesions. Intravenous pyelogram evidence of hypernephroma.

posterior mediastinal tumor probably benign. Considered were neurofibroma, dermoid cyst, pericardial cyst, esophageal cyst, tumor of diaphragm, lipoma, pleural tumors, etc. We did not think of herniated liver.

Operation was performed under nitrous oxide-oxygen and ether on Aug. 22, 1946. Incision was made along the course of the eleventh rib from the xiphoid process to the cartilage and the rib was subperiosteally resected. One inch of the eighth rib was removed anterior to the transverse process. The pleura was spread through the

In 1943, Bradley and Greiner<sup>3</sup> reported the case of an infant who at the age of weeks was found to have a mass in the right chest. The infant died of pneumonia at the age of 5½ months before the operation could be performed. The autopsy showed the right lobe of the liver and the gall bladder to be in the right chest at the height of the second rib anteriorly and covered by thin, fibrous membrane which was a defective portion of the diaphragm forming a hernial sac. In addition, there was rudimentary development of the right lung which was offered as evidence that the herniation occurred before birth.

In 1941 Wagner<sup>4</sup> reported a case in which normal liver the size of a hen's egg, herniated through the right cardiophrenic angle of the diaphragm. At operation the constricting groove was split, the hernia reduced, and phrenicotomy was done. Palpitation was the principal early symptom, but pain developed later. Neither specific attack of nausea and vomiting nor presence of strangulation were mentioned.

None of the reports mentioned a congenital veil. However it was suggested from Haeblerlin's<sup>5</sup> case that the veil is an anomaly of the diaphragm. His was a case of a 4-week-old male who died from stenosis of the cardia of the stomach and bronchopneumonia. At post-mortem examination the right pleural cavity was found divided by a membrane extending from the base of the sixth rib forward in an arc to the angle of the inferior vena cava and pericardium where it joined with the diaphragm. The base was transparent but the free margin contained striated muscle and a small nerve and blood vessel.

In the cases just reviewed the symptoms were those of pressure sensation, subternal pain, tachycardia and dyspnea. The symptomatology in our case was singularly significant and expressive and was offered spontaneously by the patient. The descriptive terms of "queezing," "ball-like" and "knotty" with cloudlike spreading from a central point beneath the xiphoid, "tense obstruction" and "door stop" feeling on bending forward and to the right created a distinct clinical impression of a diaphragmatic hernia. However when the roentgenograms were reviewed the mass was considered to be a thoracic neoplasm. As in Lillenthal's<sup>6</sup> and Wagner's<sup>4</sup> cases, the findings at surgery came as a complete surprise.

Hedblom<sup>7</sup> stated that among the cases of congenital diaphragmatic hernia there is frequently associated some other anomaly of development such as cleft palate, harelip, patent ductus arteriosus, or foramen ovale. We believe our patient has a patent foramen ovale.

In retrospect like Lillenthal, we pondered the value of pneumoperitoneum and pneumothorax as diagnostic aids. It is probable that pneumothorax would have been of no value. Pneumoperitoneum might have offered additional information and would have ever suspect diaphragmatic hernia if the liver were well up. We feel it should be tried in every suspected case because a break in the subdiaphragmatic mass would probably be roentgenologically demonstrable thus indicating that the supra-diaphragmatic mass is attached to the liver.

Since the symptoms presented by our patient were not found in the cases reported it might be questioned that our patient's symptoms were caused by the



The postoperative course was uneventful; she was ambulatory on the second day, the wound healed per primam, and she did not require thoracostoma. On the eighth postoperative day she was discharged home. Normal activities were resumed in eight weeks. The discomfort feeling disappeared, there was no more pain for fourteen months. Fluorography still showed elevated fixed diaphragm after fourteen months. The six-month follow-up ray view of the chest is shown in Fig. 4.

#### COMMENT

Our search of the literature failed to reveal any case of herniation of the liver which was strangulated, presented the symptoms of epigastric pain, nausea, and vomiting and was operated upon. Lillenthal's case reported in 1931 was the only case which closely resembled ours. His patient was a female of unstated age but probably of middle age who complained of a heaviness in the chest with slight difficulty in breathing and a slight cough, but with no gastrointestinal complaint. She was known to have had a tumor of the chest for sixteen years. The x-ray view showed a large, rounded mass occupying the lower half of the right side of the chest which was thought to be a dermoid cyst of the mediastinum. At operation there was a globular mass covered by the thin tunica of the diaphragm. The right lobe of liver was smaller than normal.

The diaphragm was paralyzed by crushing the phrenic nerve and a pleurotomy was performed. The lower part of the diaphragmatic incision was closed over the mass. This incision had been made in order to explore the subdiaphragmatic space. Reproductions of the pre- and postoperative x-ray pictures showed that the upper limit of the diaphragmatic hernia was the interapex lower following operation. This case differs from ours in not having a constriction at the neck necessitating incision in order to reduce the strangulation. This tumor was larger and consisted of all of a shrunken right lobe of liver instead of part of a normal-sized, right lobe as in our case.

In 1908, Elder and Poullethwait reported a post-mortem examination of a 57-year-old man, in which there was a large tumor in the chest consisting of liver and gall bladder covered by diaphragmatic pleura. The base of the tumor was found resting on liver beneath it and its edges attached to the remaining diaphragm all around it but no mention was made of strangulation.

In 1910, Keith reported two cases of diaphragmatic hernia discovered at post-mortem examination. One was an infant, aged 4 months, and the other a child, but these were not fully described. Their origin was attributed to abnormal liver development within the septum transversum of the embryo.

In 1938, Harrington and Kirklin reviewed 131 cases of diaphragmatic hernia and stated, "In the rare cases of the hernia through the right arch of the diaphragm a portion of the liver projects through the breach and is likely mistaken for a neoplasm." Harrington also reported upon 304 patients with diaphragmatic hernia in whom operation was performed. Only one hernia was found containing stomach, duodenum, small bowel,

In 1943 Bradley and Gleimer<sup>4</sup> reported the case of an infant who at the age of 7 weeks was found to have a mass in the right chest. The infant died of pneumonia at the age of 5½ months before the operation could be performed. The autopsy showed the right lobe of the liver and the gall bladder to be in the right chest at the height of the second rib anteriorly and covered by thin, fibrous membrane which was a defective portion of the diaphragm forming a hernial sac. In addition there was rudimentary development of the right lung which was offered as evidence that the herniation occurred before birth.

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In 1908, Elder and Postlethwait reported a post mortem examination of a 67-year-old man, in which there was a large tumor in the chest consisting of liver and gall bladder covered by diaphragmatic pleura. The base of the tumor was found resting on liver beneath it and its edges attached to the remaining diaphragm all around it but no mention was made of strangulation.

In 1910 Keith reported two cases of diaphragmatic hernia discovered at postmortem examination. One was an infant, aged 4 months, and the other a child, but these were not fully described. Their origin was attributed to abnormal liver development with ninth septum transversum of the embryo.

In 1933, Harrington and Kirklin reviewed 131 cases of diaphragmatic hernia and stated, "In the rare cases of hernia through the right arch of the diaphragm a portion of the liver projects through the breach and is likely mistaken for a neoplasm." Harrington reported upon 304 patients with diaphragmatic hernia in whom operation was performed. Only one hernia occurred on the right side and contained liver, stomach, duodenum, small bowel, and the head of the pancreas.

## LIPOMA OF THE THENAR

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(From the Department of Surgery and the Department of Pathology, The University of Oklahoma School of Medicine)

THE distribution of adipose tissue is widespread, yet in some locations neoplasms composed of adipose tissue alone, lipomas, rarely occur. One of these sites is the palm of the hand. Not counting lipomas arising in tendon sheaths of fingers, only about ten lipomas of the palm have been reported to date (Straus, Valdoni,<sup>1</sup> Pollockson, Francon, and Pizzera, Mason, and Bunnell). Few of these growths were recognized as lipomas before operative removal. The case herein reported is believed to be the first lipoma of the palm recorded in a Negro.

### REPORT OF CASE

G. R., 45-year-old Negro man, admitted to the University of Oklahoma Hospital, March 23, 1947, with the complaint of painless swelling of the left hand first noted in February 1944. The swelling was located between the thumb and the index finger and increased gradually. At present size causing progressive limitation of apposition between the thumb and fingers.



FIG. 1.—Roentgenogram of the left hand disclosing globular soft tumor mass between the first and second metacarpal bones (the lower digit) the one surrounding of thumb thought to be lipoma.

At the time of admission the patient appeared to be in good health. The only positive finding was ballotable soft mass between the left thumb and index finger limited to the thenar area and elevated 2.5 cm. low the palmist and 1.5 cm. over the dorsal surface. The skin over the mass was smooth, somewhat stretched, movable and not tender or painful. The mass did not transmit light. The thumb and index finger could not be opposed. Roentgenographic examination disclosed globular soft tissue mass between the first and second metacarpal bones, the lower density than the surrounding soft tissues. The mass was thought to be lipoma (Fig. 1).

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herniated liver. We suspect that the absence of these symptoms in the cases previously reported can be ascribed to the absence of strangulation of the liver. Therefore, we feel that the attacks of pain, nausea, and vomiting were related to the strangulation. The absence of any abnormalities in the x-ray examinations of the esophagus, stomach, small and large bowel, biliary tract, and genitourinary tract, together with the disappearance of symptoms following operative reduction of the strangulated liver, lends credence to the idea that the syndrome described was in fact related not so much to the constantly present hernia of the liver but rather to its periodic strangulation.

The conception that this type of hernia is congenital indicates that the herniation of the liver was present since birth but it is probable that the strangulation first occurred with the onset of the attacks six months before operation. The associated pleural veil obviously a congenital malformation, as well as the atrial septal defect in the heart are further evidence for the congenital origin of this hernia of the liver.

#### SUMMARY AND CONCLUSIONS

A case of congenital, strangulated, diaphragmatic hernia of the liver with surgical cure is reported. This case included a unique symptomatology of attacks of nausea, vomiting, and epigastric pain described as cloud like with radiation to both lower lateral thoracic areas. A doorstop feeling on bending forward was a prominent feature of the symptomatology. These symptoms probably have a causal relationship to the strangulation of the herniated liver and with the surgical reduction of the hernia the patient experienced a complete and lasting cure. When a mass is radiologically demonstrated in the pericardiophrenic sulcus, herniation of the liver should be considered as well as the more common lesions. If abdominal symptoms of the type described herein are present, it is reasonable to suspect strangulation of the herniated liver and exploratory thoracotomy should be advised.

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# LIPOMA OF THE THUMB

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THE distribution of adipose tissue is widespread, and in some locations neuromas composed of adipose tissue alone (lipomas) rarely occur. One of these sites is the palm of the hand. Not counting lipomas arising in tendons (sheaths of fingers), only about ten lipomas of the palm have been reported to date (Strauss, Valdoni, Pollockson, Francon, and Pizzero, Mason, and Bunnell). Few of these growths were recognized as lipomas before operative removal. The case herein reported is believed to be the first lipoma of the palm recorded in a Negro.

## REPORT OF CASE

C. R., 40-year-old Negro woman, was admitted to the University of Oklahoma Hospital, March 23, 1941, with the complaint of a painless swelling of the left hand first noted in February 1941. The swelling was located between the thumb and the index finger and increased gradually to its present size causing progressive limitation of apposition between the thumb and fingers.



FIG. 1.—Roentgenogram of the left hand disclosing a globular soft tissue mass between the first and second metacarpal bones with lower density than the surrounding soft tissue thought to be lipoma.

At the time of admission the patient appeared to be in good health. The only positive finding was a ballot like soft mass between the left thumb and index finger limited to the first area and elevated 2.5 cm. above the palmar and 1.5 cm. over the dorsal surface. The mass was smooth, somewhat stretched, movable and not tender or painful. The mass did not transmit light. The thumb and index finger could not be apposed. Roentgenographic examination disclosed a globular soft tissue mass between the first and second metacarpal bones with a lower density than the surrounding soft tissue. The mass was thought to be a lipoma (Fig. 1).

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herniated liver. We suspect that the absence of these symptoms in the cases previously reported can be ascribed to the absence of strangulation of the liver. Therefore, we feel that the attacks of pain, nausea, and vomiting were related to the strangulation. The absence of any abnormalities in the x-ray examinations of the esophagus, stomach, small and large bowel, biliary tract, and genito-urinary tract, together with the disappearance of symptoms following operative reduction of the strangulated liver, lends credence to the idea that the syndrome described was in fact related not so much to the constantly present hernia of the liver but rather to its periodic strangulation.

The conception that this type of hernia is congenital indicates that the herniation of the liver was present since birth, but it is probable that the strangulation first occurred with the onset of the attacks six months before operation. The associated pleural veil, obviously a congenital malformation, as well as the atrial, septal defect in the heart are further evidence for the congenital origin of this hernia of the liver.

#### SUMMARY AND CONCLUSIONS

A case of congenital strangulated, diaphragmatic hernia of the liver with surgical cure is reported. This case included a unique symptomatology of attacks of nausea, vomiting, and epigastric pain described as cloud like with radiation to both lower lateral thoracic areas. A doornop feeling on bending forward was a prominent feature of the symptomatology. These symptoms probably have a causal relationship to the strangulation of the herniated liver and with the surgical reduction of the hernia the patient experienced a complete and lasting cure. When a mass is radiologically demonstrated in the pericardiophrenic sulcus, herniation of the liver should be considered as well as the more common lesion. If abdominal symptoms of the type described herein are present, it is reasonable to suspect strangulation of the herniated liver and exploratory thoracotomy should be advised.

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Herniability of the Liver Encapsulating

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# LIPOMA OF THE THENAR

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THE distribution of adipose tissue is widespread, yet in some locations neoplasms composed of adipose tissue alone (lipomas) rarely occur. One of these sites is the palm of the hand. Not counting lipomas arising in tendon sheaths of fingers, only about ten lipomas of the palm have been reported to date (Strauss, Valdoni, Pollockson, Francon, and Pizzera, Mason, and Bunnell). Few of these growths were recognized as lipomas before operative removal. The case herein reported is believed to be the first lipoma of the palm recorded in a Negro.

## REPORT OF CASE

A 40-year-old Negro male admitted to the University of Oklahoma Hospital, March 7, 1944, with the complaint of painless swelling of the left hand, first noted in February 1944. The swelling was located between the thumb and the index finger and increased gradually to its present size causing progressive limitation of apposition between the thumb and fingers.



Fig. 1.—Roentgenogram of the left hand disclosing glomerular soft tissue mass between the first and second metacarpal bones with lower density than the surrounding soft tissue thought to be lipoma.

At the time of admission the patient appeared to be in good health. The only positive finding was a ballotable soft mass between the left thumb and index finger limited to the

thenar  
area  
discovered  
graphically  
carpal

to be lipoma (Fig. 1)

and the full underlying soft tissues. The mass was thought



Under regional nerve block anesthesia with procaine (1 per cent) and after application of pneumatic tourniquet over the arm, incision 9 cm. long was made along the thenar crease. The skin with the fascia reflected radially. The thenar muscles were incised parallel to their fibers exposing globular encapsulated, yellow mass, apparently composed of adipose tissue. After freeing of the palmar portion and separation from its attachment to the tendon sheath of the flexor pollicis longus, pressure on the dorsal extension of the mass delivered it into the wound. Following removal of the tourniquet, bleeding was slight. After hemostasis the wound closed in layers and pressure bandage applied. Healing of the wound as uneventful. When the patient last seen, Aug. 21, 1947, the three areas were symmetrical and there was no impairment of the function of the thumb and fingers.

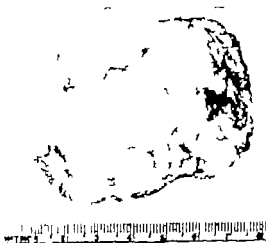


Fig. 2.—Lipoma of the thenar. The growth is composed entirely of rounded lobules of adipose tissue.

The specimen consisted of slightly lobulated globular mass of adipose tissue 1 by 3 by 2 cm. and weighing 50 Gm. (Fig. 2). A delicate transparent capsule surrounded the mass. The rounded lobules on its surface measured 1 to 4 cm. in diameter. The cut surfaces were yellowish white. Microscopic preparations from various

#### SUMMARY

A lipoma of the thenar in a 40-year-old Negro woman is reported. This apparently is the eleventh lipoma of the palm and the first such growth recorded in a Negro.

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## THE DILUTE PENTOTHAL DRIP INFUSION

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WE AND our associates have been administering pentothal sodium in very dilute solution as a drip infusion during the past two years in over 5000 cases. It has proved to be so widely and variously useful that we believe it deserves greater popularity.

Solkow and Clement<sup>1</sup> in 1941 were the first to report the drip infusion of 1:200 and 1:100 solutions of pentothal for complete intravenous anesthesia. Lepowitz, Lapson, and Stevens, in 1944 described the infusion of 1:1000 and 1:500 Pentothal sodium for sedation and narcosis. Their excellent experience with high dilutions in 51 patients undergoing surgery under spinal, regional, and local anesthesia provided a physically easier and clinically safer method for the greater application of the virtues of the more concentrated solutions of pentothal sodium recommended as an adjunct to regional anesthesia by earlier authors.<sup>2-4</sup> Steven<sup>5</sup> used various dilutions of Pentothal sodium, 1:250 for complete anesthesia, 1:500 and 1:1000 for sedation or hypnosis in good risk patients, and basal anesthesia in poor risks. He confirmed the fact of safety, sterility, and the persistence of potency of these solutions in bulk kept for five days or more. The dilute pentothal drip was then such an innovation that Adams, in his extensive review of the literature published in 1944, did not refer to the use of such a dilution.

### TECHNIQUE

The standard solution always on hand is 1:1000. The choice of the concentration of Pentothal sodium, varying from 1:2000 to 1:500 must be guided by several factors: (a) the depth of sedation, narcosis, or anesthesia desired; (b) the anesthetic resistance and the effect of premedication; (c) the total volume of fluid considered optimum; (d) the size of the needle and the desirable rate of flow of the infusion. As a rule the needle is 20 gauge, the concentration is 1:1000 and the total volume infused for sedation is 200 to 400 cc. for basal anesthesia 300 to 1000 cc.

For a short complete anesthesia with pentothal we still prefer the intermittent injection of 5 per cent. For complete anesthesia with pentothal for a long period of time when the intermittent method might be inconvenient and tiresome we now prefer the drip method, with 1:500 to 1:1000 pentothal to the intermittent injection of the 5 per cent concentration after the first hour when the patient has settled down to requiring only small amounts per hour. The earlier experience of the senior author with the use of Pentothal sodium in special cases and for prolonged surgery<sup>6</sup> enables us to appreciate more clearly the convenience, comfort, and careful control provided by the dilute pentothal drip.

Pentothal is dissolved usually in five per cent glucose in saline solution for the eclamptic cardiac, or other disease states in which saline solution is contraindicated the solvent is 10 per cent glucose in distilled water.

#### INDICATIONS AND ADVANTAGES

1. *As Sedative or Hypnotic in Spinal Anesthesia*—The most frequent indication for 1 1000 Pentothal sodium solution is sedation and light hypnosis during spinal anesthesia. Whereas we and practically all of our surgeons prefer and use spinal anesthesia in the great majority of operations below the diaphragm most patients desire to be asleep during the operation. Pentothal, 50 to 200 cc of 1 1000 solution produces a drowsy or lightly sleeping patient within 5 to 15 minutes, depending on the preoperative effect of the usual premedication. Drowsiness by properly timed and chosen premedication is frequently not attained because of special circumstances, for example a delay in the operating room schedule, insufficient time before emergency operation, individual differences in response personal preferences of a surgeon, etc. In the past intravenous morphine sulfate with or without scopolamine hydrobromide was used to correct these inadequacies in premedication. With 1 1000 Pentothal sodium one can obtain a calm quiet, drowsy patient more promptly and reliably. After the loss of the corneal reflex, the rate of flow is slowed to maintain sleep in deep first stage anesthesia. The patient avoids unpleasant memories and is indifferent to the discomforts of the operating table, for example the pressure of the shoulder guards in deep Trendelenburg position, and the prolonged immobility of arms and head during lengthy operations. The accurate control of certain sleep has enabled us to increase our service to the surgeons by using spinal anesthesia in a great percentage of cases. The private patient who used to refuse spinal anesthesia now accepts it willingly if promised a pleasant induction of sleep. The dilute pentothal drip enables one to produce sleep, if necessary, after lumbar puncture without the assistance of another anesthetic and without fear of the respiratory obstruction and depression possible with 5 per cent Pentothal sodium administered to a patient in the lateral position after lumbar puncture. The surgeon who, for one reason or another, used to praise his patient for being asleep during operation is pleased to secure the incomparable advantages of spinal anesthesia without the disadvantages of inhalation anesthesia. The infusion of pentothal has the following advantages over inhalation anesthesia as a supplement to spinal anesthesia:—

(1) it is not irritating (2) it is not very far from sleep in contrast to the inhalational agent (3) it is not economical (4) it does not demand an anesthetic machine thereby freeing the latter for other cases.

It is the agent par excellence to supplement spinal anesthesia which is unavoidably complicated, at times, by painful traction reflexes mediated by spinal and phrenic pathways. Pulling on the gall bladder, liver, stomach, esophagus,

or diaphragm is often accompanied by retching or vomiting making the patient miserable and the surgery more difficult if not impossible. The situation can be remedied promptly and reliably by 100 to 300 c.c. of 1:1000 pentothal; the patient and the surgical field become quiet often before the patient goes to sleep.

The dilute pentothal infusion lends itself to avoiding overdosage with general anesthesia when the latter is utilized as a supplement to spinal or regional analgesia. It is the rule to see the patient reacting vigorously in the operating room even after three hours of sleep with very dilute pentothal solutions.

*Is a Basal Anesthetic.*—The dilute drip is a more precise method of producing a minimal level of general anesthesia with or without supplementary agents. In this way one can more safely give the small fractionally administered doses of 0.1 to 0.3 Gm. of Pentothal sodium needed, for example, in borderline shock or during the unpleasant moments of resection of tumor or pinning of the hip under local anesthesia.

*Is an Anti-thyrotic Agent.*—All of our hyperthyroid patients except burnt out ones (who are very susceptible to any depressant agent) are carried through operation with basal anesthesia produced by an infusion of 1:1000 Pentothal sodium started either in the operating room or occasionally in the patient's room if concerned the impending operation. Unlike tribromethanol, dilute pentothal does not produce respiratory or circulatory depression. Better than tribromethanol it antedotes thyrotoxic effects on metabolism and circulation. The value of Pentothal sodium for the antagonism of thyroid toxicity during operation may be continued after operation when a thyroid storm is considered to be a likely sequel. Hudson's experience in 600 cases with Pentothal in surgery for hyperthyroidism has shown its anti-thyrotic value. With pentothal basal anesthesia a postoperative thyroid storm has never occurred in our experience. In the few cases of severe hyperthyroidism which were not for reasons beyond our control, anesthetized with Pentothal sodium, we have secured, with a dilute pentothal infusion, excellent control of thyroid toxicity after operation. The postoperative sleep, accurately and quickly regulated at a light level with active throat reflexes, is better obtained with 1:1000 pentothal than with the traditional but improperly indicated postoperative morphine. Hudson, using 5 per cent pentothal as the complete and sole anesthetic agent encountered respiratory depression in several cases. Dilute pentothal has made it easy to avoid this undesirable state.

*Is Depressant of Excessive Sympathetic Nervous System Activity.*—The apprehension and excited sensibility of some patients during regional anesthesia are at times engendered by an excessive use of, or reaction to the epinephrine injected with the anesthetic drug. Barbiturates are excellent antagonists for generalized sympathetic nervous overactivity. Pentothal is one of the most controllable of all barbiturates, especially in a very dilute solution. Therefore we regard the dilute pentothal drip as the indicated means of solving an unpleasant situation created by a fearful and anxious patient complaining of every touch, restless jittery and twitching during an otherwise satisfactory regional block. Another indication for the use of the special ability of pentothal to depress excessive sympathetic stimulation is to induce general

anesthesia in the patient whose sympathetic nervous activity is at a peak as a result of painful surgery with an inadequate cocaine surface anesthesia and epinephrine stimulation in the presence of an unsuccessful or waning spinal anesthesia. Under these and similar circumstances cyclopropane might be dangerous because of cardiac hyperirritability and nitrous oxide or ethylene too weak to overcome without severe anoxia the greatly increased metabolic level.

The dilute pentothal drip is the safest and most practicable means of combating the transient hypertension and severe headache occasionally seen as an excessive response to the vasopressor drugs, neosynephrin or epinephrine especially with posterior pituitary extract during spinal anesthesia.

5 *In Cardiac Patients*—The dilute pentothal drip is a precise and very convenient method for the induction of general anesthesia in cardiac patient when premedication has failed to produce the needed degree of sedation for safe induction with the inhalational agents. The dilute pentothal drip is without effect on the heart and peripheral circulatory mechanism, and avoids the disadvantages of cyclopropane effects on cardiac irritability of anoxia with nitrous oxide or ethylene and of prolonged excitement with ether. For special protection against undue cardiac irritability, procaine hydrochloride may be added to the pentothal infusion, as suggested by Kraft. Thus, procaine 1:1000 and pentothal 1:1000 may be mixed and administered in the same solution. Precipitation does not take place between the two drugs in 1:1000 concentrations. The dilute pentothal drip is particularly useful as a vehicle for intravenous procaine. The safety of intravenous procaine, primarily dependent on high dilution and slow administration is enhanced by the pentothal hypnosis. The pentothal may be discontinued after induction in favor of ether the agent of choice for maintenance of anesthesia in cardiac patients, or the pentothal may be neatly combined with safe concentrations of nitrous oxide or ethylene and oxygen with curare if necessary for relaxation. Curare solutions may be injected directly into the tubing containing dilute pentothal with negligible precipitation and without any noticeable decrease of curare effect.

6 *As a Means of Administering Pentothal Outside of the Operating Room*—The acknowledged superiority of pentothal for the control of convulsions has been safely and readily adapted, by means of the dilute infusion, to the cases of eclampsia before, during and after cesarean section. Similarly we have easily controlled convulsions arising from cerebral damage by anoxia as a result of circulatory failure during spinal anesthesia.

The dilute penthal drip is the only safe and practicable way of administering pentothal for a prolonged period of time in the patient's room. By alternating two connected infusion solutions, one of dilute pentothal and the other without pentothal sleep or sedation has been nicely continued for many hours on the ward. Of course this form of hypnosis or sedation is utilized only for serious or special conditions, when the patient is under continuous, intelligent and instructed medical and nursing supervision.

#### CONTRAINDICATIONS AND PRECAUTIONS

Dilute pentothal is not an analgesic. It is not an efficient substitute for poor regional or spinal analgesia. It should not be used to stop nausea or con-

ring resulting from a fall of blood pressure for this the choice is intravenous ephedrine or restoration of blood volume depending on the cause. Pentothal is not employed when hypoxia of any origin is the reason for a complication. Even a small volume of 1-1000 Pentothal sodium has caused apnea during high spinal anesthesia in a good risk patient. The high dilution does not eliminate the precautions associated with the proper use of intravenous anesthesia.

Dilute pentothal for basal anesthesia requires the same preoperative attention to adequate premedication with atropine as has been found desirable with 5 per cent pentothal if one is to avoid excessive bronchial secretion, laryngospasm, and hiccup.

The first postoperative dose of morphine should be one-third to one-half less than usual for the patient who has received a dilute pentothal solution. Even the administration of 0.3 to 0.5 Gm. Pentothal sodium during one to two hours leaves a postoperative sedative effect as shown by an increased susceptibility to respiratory depression by morphine and a decreased tendency to vomit.

#### SUMMARY AND CONCLUSION

The dilute pentothal drip infusion is a handy adaptable precise and economical method of utilizing the special qualities of Pentothal sodium before, during and after operation. The valuable characteristics which are made more evident and widely useful by the highly dilute solution of Pentothal sodium are (1) sedative and hypnotic (2) basal anesthetic (3) anticonvulsant (4) antiemetic (5) antithyrotic and (6) depressant of excessive sympathetic stimulation.

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## A NEW LAMINECTOMY RETRACTOR

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A LAMINECTOMY retractor to be satisfactory must be constructed so that it can be easily and quickly inserted and stable enough to resist the strong pull of the paravertebral muscles when they have been displaced laterally. A retractor has been devised which meets these requirements. The simplicity of its design is the result of improvement or elimination of several cumbersome features of earlier models which we made.

The instrument consists essentially of two sets of parts: the retractor blades and a rectangular frame to hold and to spread them. The frame (Fig. 1) is made of two parallel square brass bars; one of these has two round solid rods screwed into it and the other is fitted with two tubes which serve for reception of the round rods. The rods fit into the tubes just loosely enough to permit easy extension of the frame. The tubes are tightly fitted through holes in one of the square bars and soldered in place.

The locking device (Fig. 1) is made of two short pieces of slightly curved spring steel. Drilled through each spring is a hole with a diameter slightly larger than that of the solid rod; the spring being attached with two screws on the outside of the bar bearing the tubes. This lock allows the rods to be pulled through as the frame is spread open but rigidly resists closure of the frame unless pressure is applied with the fingers on the free ends of the springs. This lock has proved to be efficient and has the advantage of being easily released.

There are three sets of retractor blades differing only in length. The one to be used is determined by the thickness of the tissues to be retracted. The

through it and soldered for increased rigidity. Each of the bars of the retractor frame has five holes reamed with a No. 6 taper bit. This arrangement allows the individual blades to be easily placed directly opposite the vertebral laminae or intervertebral ligaments which are to be approached surgically. The frame is then placed over the blades and the tapered pins are guided into the closest holes. Slight pressure on the frame then locks the blades in place. One of the greatest advantages of this instrument is its adaptability for insertion of the blades where retraction is most needed.

The dimensions and shape of the components of the retractor are accurately indicated in Fig. 1. Our instrument was made of brass because of the ease with

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which that metal can be machined. A skilled machinist could make a lighter and stronger one of stainless steel.

The retractor functions equally well for unilateral or bilateral laminectomy. If a hemilaminectomy is to be performed, only one blade is placed on the opposite side. The lumbar dorsal fascia of that side is separated from its attachment by an incision just long enough to slip a single blade past it to occupy a position comparable to that of blades on the side of the operator. Thus, the instrument is as hored as firmly as if laminas were being exposed bilaterally and the tissues of the opposite side are subjected to a minimum of trauma. On the close of the operation retractor blades are placed directly opposite the lamina or ligamenta flava in question; this assures maximal retraction at the point

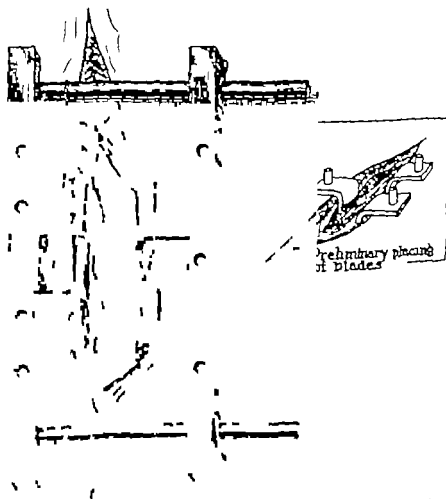


Fig. 2.—Retractor in place for hemilaminectomy. Lower shows blades in position before the retractor frame is placed over them.

desired point. A blade of such length that it will pass laterally along the transverse process and at the same time allow the frame of the retractor to fit firmly against the skin is used. Retractor frames shaped to fit more accurately the lordotic curve of the lumbar and cervical regions and the kyphotic curve of the thoracic region have been designed. The position of the blades at right angles to the long axis of the muscles to be held aside provides satisfactory retraction with separation of the lumbodorsal fascia and adjacent muscles from their attachment for a relatively short distance so that operative trauma is further minimized. The fact that one or several blades may be used on each side also permits exposure of the area without undue disturbance of overlying tissues. The number of blades used on one side (one to five) is determined by the size of the area to be exposed.

This instrument has proved to function satisfactorily. The simplicity of its design and action assures a minimum of difficulty in its use.

## Case Reports

### APOPLEXY OF THE GALL BLADDER

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THE purpose of this communication is to report an extremely rare condition, in which there was a large hemorrhage into the noncalculous gall bladder of a patient with essential hypertension. A search of the literature has failed to disclose an identical case.

*Hemocholeyst* is the term applied by Pieminger<sup>3</sup> to massive, non-traumatic gall bladder hemorrhage. We have employed the term *apoplexy of the gall bladder* in the case herewith presented as there was hypertension and absence of gallstones.

It is thought likely that light bleeding may occur frequently in diseased gall bladders. Hudson and Johnson found blood in the stools in 13 per cent of 100 consecutive cases of cholelithiasis in which operation was required and in 8 per cent of 100 cases of cholecystitis without cholelithiasis. A massive hemorrhage in the belief of most early writers, is due to infection. However a large hemorrhage may also be due to trauma,<sup>4</sup> a tumor rupture of an aneurysm of the cystic artery or some other intrinsic pathological changes in the blood vessels. Hudson and Johnson found that sclerotic changes were present in their 4 cases and considered these significant, with mechanical irritation from stones being of secondary importance. Pieminger stated that the causes of the hemorrhage are processes, either toxic or irritative which are capable of producing superficial and deep vascular ruptures.

A large hemorrhage may remain localized to the gall bladder, it may diffuse through the bile duct into the bowel causing melena or hematemesis, or it may produce sufficient pressure within the gall bladder to rupture the viscus and permit free bleeding into the peritoneal cavity.

If traumatic cases are excluded, massive hemorrhage from the gall bladder is almost always associated with cholelithiasis. On reviewing the literature,<sup>23</sup> such cases were found to have been reported. However massive hemorrhage from a noncalculous gall bladder is very rare. In addition to the case herewith presented only two other cases have been reported, one by Schnyder<sup>2</sup> concerning a man aged 77 years, and one by Pieminger<sup>3</sup> concerning a boy aged 4½ years.

Hypertension has been noted in only one other case of massive hemorrhage that of Hudson and Johnson, the blood pressure being 185/104 but in their case cholelithiasis was present.

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## REPORT OF CASE

Mrs. A. M., 46-year-old housewife, admitted to F. Austin Hospital, January 18, for observation and treatment of essential hypertension of 10 years duration. The systolic blood pressure slowly dropped from 230 to 170 with the diastolic pressure remaining around 150. No symptoms of gall bladder disease were noted.

The second admission was on Oct. 3, 1940. She had been at 3 o'clock that morning feeling as well as usual, but one hour later had reawakened with sudden excruciating pain in the epigastrium. A physician gave her  $\frac{1}{2}$  gr. of Pantopon, with only slight relief, and she was transferred to the hospital. The temperature was 98.5° F., the pulse 100, and the respiratory rate 20. The last blood cell count was 15,000 and the urine showed 1 plus albumin and few white and red cells. The left heart border was 11 cm. from the midclavicular line and the blood pressure was 250/160. Examination of the abdomen revealed tenderness and almost boardlike rigidity in the right upper quadrant and a slight lower extent in the left upper and right lower quadrants. The preoperative diagnosis was perforated peptic ulcer. Operation revealed an enormous distended turgid, almost blue-black gall bladder. There was also some oozing motion under the peritoneum surrounding the common bile duct and lymphatic structures and a small amount of blood-tinged fluid found in the peritoneal cavity. Cholecystectomy was performed. The patient was discharged from the hospital eight days later after uneventful postoperative course.

On gross examination in the pathology laboratory the lumen of the gall bladder appeared to be filled with blood and no calculi were found. The mucosa was markedly hyperemic and showed marked cholesterol. Small hemorrhages were scattered throughout the wall, but in one area 3.5 by 1 cm. near the base of the fundus the wall was thickened, and there was gross hemorrhage. The mucosal folds were varying 1 by 1.5 cm. No nervousness of the cystic duct was demonstrated, and no evidence of infection was seen. Microscopically congestion and hemorrhage in the wall and the lumen were observed. Scattered areas of chronic cellular infiltration and some fibrosis of the wall were noted.

On Nov. 20, 1940, forty days after the patient's discharge from the hospital, she was readmitted because of severe frontal and occipital headaches, diplopia, and pupillary changes. The blood pressure on admission was 174/108 and rose to 210/140 in spite of treatment with and the administration of bromides and Veronal. On December 1, she became comatose and finally stuporous and died on December 5. Six weeks after diagnosis and the fourth year of the essential hypertension. The most significant findings on postmortem examination are general arteriosclerosis including the brain, arterio-sclerotic kidneys with arterio-sclerosis and small multiple infarcts in the brain.

Comparison of the topographic findings in the small caliber vessels of the kidney, aorta, and brain with those in the vessels of the surgically removed gall bladder are of interest. In the gall bladder the prearteriolar and arteriolar changes were those of collagenous intimal thickening. The small vessels of the subcutaneous region of the thrombo-arteriosclerosis were seen. Most vessels so involved had lumen which were stenosed almost to the point of occlusion. Larger vessels were affected also. Although the internal elastic proliferation and other arterio-sclerotic features were prominent (especially in the renal, aortic, and cerebral vessels of small caliber shown lesions corresponding to those described in the gall bladder except that the intimal changes were pronounced). Tissues from the other organs showed comparable effect and are compatible with the diagnosis of essential hypertension.

## CONCLUSION

A case of essential hypertension is reported in which there was a massive hemorrhage into a non-neoplastic gall bladder.

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# PERFORATION OF THE SIGMOID FOLLOWING ENEMA

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**P**ERFORATION of the colon has been reported in the literature many times and has received detailed attention in the textbook of surgery. Among the etiologic agent and factors incident in this pathology are compressed air, enema nozzles, foreign bodies inserted into the rectum or taken by mouth, proctoscopes, sigmoidoscopes, bullets and other projectile objects, intestinal obstruction usually in the distal part of the large bow where the peristaltic movements may increase the intraluminal gas pressure to such an extent as to cause a rupture and blows and other injuries to the abdominal wall. Other conditions which have been mentioned include diverticula, polyps, malignant tumors, and inflammatory lesions such as typhoid fever, amoebiasis, perisigmoiditis, and ulcerative colitis.

Intestinal perforation following the administration of an enema has on the other hand appeared in the literature but rarely. In the few times that such reports have been made it was usually the enema tip or nozzle plus the forceful insertion of the same that has been at the basis of the rupture. Rappert emphasized this as did Menckhaus.

In the only case comparable to the one herein reported that we have been able to find, Hawkes discussed the instance of a patient who administered an enema to himself by attaching a soft rubber tube to the faucet of a bathtub, inserted the tube into his rectum and turned on the water. The amount of water to be given was judged by the man's intestinal sensations. The practice was repeated without harm many times until one morning he gave himself a double administration followed by a perforation of the sigmoid colon.

He was operated upon six hours after the rupture had occurred. The perforation was repaired and a proximal colectomy performed. The patient was discharged in good condition after forty-six hospital days with a moderate amount of drainage from the incisional wound and from the colectomy.

In the case that follows the perforating force apparently was not produced as in this instance by direct flow of the enema fluid but by postural increase in intraabdominal pressure.

## REPORT OF CASE

**B. M.** 52-year-old white man, born Switzerland and baker by profession, was admitted to the hospital on May 11, 1947. He was observed in great distress and complained of severe generalized lower abdominal pain. About 8 hours prior to admission he had given himself an enema consisting of about two quarts of soapy water from the usual type enema can attached by rubber tube to hard rubber nozzle. (The patient stated he had been in the habit of giving himself enemas for many years for reason not immediately apparent as to *check himself out*.)

Following the removal of the enema tip the patient described to him the fluid for while. He sat on the edge of the bathtub and leaned forward. A few moments after this he

as seized with lancinating pain in the left lower quadrant and was not able to pass any of the excess fluid. The patient went to bed and when the pain did not decrease in severity he called a physician about three hours after the episode.

Past history and systemic review are essentially negative as far as abdominal operation in another hospital some fourteen years previously following laceration in the upper part of the abdomen. Constipation is apparently uncorrected. There was no history of constipation or diarrhea, weight loss, black or bloody stools.

Physical examination revealed an obese but well-complaining female with severe abdominal pain. The face was flushed and warm and there was profuse diaphoresis. The temperature was 100° F, pulse 110 respirations 20, and blood pressure 120/70. The heart and lungs were clinically normal.

The abdomen was rigid in appearance and prevented for inspection. It healed upper middle near. Rigidity and distention were prominent and generalized. The peritoneal signs as tympany throughout. Both lower quadrants were tender to palpation, the left being somewhat greater than the right. Rebound tenderness was not elicited over the lower abdomen. Auscultation revealed complete absence of bowel sounds. There was no tenderness over the costovertebral angles.

Neurologically and skeletally, the patient presented no abnormalities.

Laboratory data showed but blood count of 7,100 with 83 per cent polymorphonuclear leukocytes, 12 of which were early forms and 12 per cent mononuclear cells. Red blood count was 4,100,000 with 93 per cent hemoglobin (H-b). Urine was straw colored and had specific gravity was 1.020 and it was found negative for sugar, proteins and inflammatory cells.

A Miller-Abbott tube was inserted and the patient brought to the operating room at 8 A.M. seven hours following onset. Anesthesia was spinal (Pentacaine).

The abdominal wall was incised and the patient brought to the operating room at 8 A.M. seven hours following onset. Anesthesia was spinal (Pentacaine). The abdominal wall was incised and the patient brought to the operating room at 8 A.M. seven hours following onset. Anesthesia was spinal (Pentacaine). The abdominal wall was incised and the patient brought to the operating room at 8 A.M. seven hours following onset. Anesthesia was spinal (Pentacaine).

As much of the fluid as possible was removed by suction. The small bowel was greatly distended and perforated throughout.

The peritoneum was explored and after considerable mechanical difficulty because of the distention and the patient's obesity, perforation on the free or antimesenteric border of the sigmoid colon was found. It measured about 3 cm in length and was located just above the peritoneal reflection on the posterior border of the bladder on the pelvic brim. The surrounding serosa was purplish black color and mottled in appearance for distance of about 10 cm from the circumference of the rupture. (It looked like powder-burn around a wound from a bullet that has been fired from close range.) There was no evidence of distention or other pathologic lesion at this site. Further exploration of the abdominal contents was not attempted.

The perforation was closed with one layer of non-absorbable plus suture. A large cigarette drain was placed in the cul-de-sac and brought out through the lower angle of the incision. The abdomen was then closed in layers using chromic suture for the peritoneum and silk for the skin.

The abdomen was re-draped, McBurney's incision was made in the right lower quadrant and the patient was brought to the operating room at 8 A.M. seven hours following onset. Anesthesia was spinal (Pentacaine). The abdominal wall was incised and the patient brought to the operating room at 8 A.M. seven hours following onset. Anesthesia was spinal (Pentacaine).

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intravenously and the patient given 50,000 units of penicillin and 400 mg. of streptomycin every three hours.

The patient's temperature rose to 101° F. on the first postoperative day and then gradually fell to normal eleven days following surgery.

Blood, 500 cc. was given on the second postoperative day. About reaction half dosage discontinued five days. penicillin and streptomycin after ten.

Distention disappeared on the third day. The patient had three small bowel movements on the fourth and was out of bed on the sixth day. The Miller-Abbott tube had been removed the day previously and the catheter brought out of the rectum one week after the operation.

Recovery from the operation uncomplicated. Drainage from the incision was minimal and finally stopped altogether in two weeks about the same time that the rectostomy closed on and began to heal spontaneously.

The patient was discharged symptomatic on the twenty-first hospital day.

#### COMMENT

This case illustrates many of the features that have been delineated in the literature in the past concerning sudden perforation of the large intestine. So far as can be determined, however, it is the first instance recorded of a perforation following an enema after the enema apparatus had been removed and in which the patient had retained the fluid. Somewhat noteworthy too was the rapid convalescence following an episode of such gravity.

Colonic ruptures are always pernicious because of the highly pathogenic bacterial flora which gain access to the free peritoneal cavity. Mortality in several series of rupture has varied between 50 and 100 per cent, most of these following pneumonic perforation of the colon.

An enema of course gaining access to the free abdominal cavity offers a vehicle for wider dissemination of fecal material and the prognosis must subsequently be more guarded.

In the series of operative cases cited by Hays, the site of pneumonic rupture was the sigmoid in ten instances, the cecum in one, the hepatic flexure in one and the rectum in two. The sigmoid is most involved doubtless because of its anatomic position. The rectum is a relatively fixed organ and well protected, while the sigmoid is the first freely movable part of the large bowel that is encountered in distal to proximal direction. Then too the sharp curve it describes is probably contributory to making it the most common site of traumatic rupture in which retrograde force is the etiological factor. Andrews has shown experimentally that it took only seven to twelve and one-half pounds of pressure to rupture a piece of human intestine.

From a gross pathologic point of view the powder burn appearance of the serosa immediately adjacent to the perforation is characteristic and offers a ready means of discovering the site of lesion, especially in patients on whom surgery is mechanically difficult—who are obese and who present evidences of marked distention as did the one just reported.

The history is usually readily obtained and characteristic. Pain is the first symptom complained of in a majority of cases and usually comes on suddenly although in a few instances it has not occurred for an hour or two following the exciting force. The pain is continuous in character and severe. The patient is restless and anxious. The abdomen is tense, rigid, and exhibits rebound phe-



nominal ventilation reveals absence of peristalsis after the lapse of a few hours. The temperature at first is usually normal, subnormal, or only mildly elevated. The white blood count commonly rises to 15,000 to 18,000 although in the current instance it remained normal, showing a shift to the left in the differential calculation.

In Hawkes' case and in the present one the surgical approach was identical. In the current one however the period of convalescence and time for healing were just about halved. This undoubtedly follows from the newer knowledge of nutrition, protein balance, the use of vitamin C and of the chemotherapeutic drugs. The question of drainage remains in abeyance. In this case no deleterious effects were noted.

#### SUMMARY

1. A case of traumatic perforation of an apparently nonpathologic sigmoid following self-administration of an enema has been presented. The enema fluid was retained and rupture followed sudden increase in intra-abdominal pressure occasioned by the patient's bending over.

The signs and symptoms following traumatic colonic perforation have been outlined and the salient anatomic, physiologic, and pathologic factors enumerated.

2. The literature has been reviewed.

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 A New Type of Industrial Air

# Editorial

## Why Treat Gastric Ulcers Medically?

IT WOULD seem that sufficient evidence has now been accumulated to justify the conclusion that gastric ulcer should always be treated surgically unless the individual physical condition makes this inadvisable. It is a well known fact that the medical profession is slow to discard any well-established therapeutic procedure so it is not surprising to note that many still cling to the belief that, initially at least gastric ulcer is a medical problem. The evidence in favor of surgery is so overwhelming that it would seem justifiable to present again the subject for the benefit of those who still favor conservatism. The gradual realization of two indisputable facts is responsible for the changed attitude toward the therapy of gastric ulcer.

First, there is at present no known method or methods by which one can differentiate between a benign and a malignant ulcer and second, the morbidity and mortality following resection for gastric ulcer in competent hands are remarkably low.

No one, however well trained in x ray interpretation or gastroscopic examination or any method of investigation known at the present time can tell whether a gastric ulcer in its early stages is benign or malignant. The gross appearance of the ulcer after removal is frequently noncommittal and only by careful microscopic examination can its true nature be determined. All pathologists of experience recall instances where only a small area of the wall of the ulcer showed the characteristic appearances of malignancy.

Just what percentage of benign ulcers ultimately undergo malignant degeneration cannot be accurately determined. An individual proved to have gastric malignancy not infrequently gives a history of years of epigastric distress suggesting ulcer and occasionally in addition, there has been x ray evidence to support this diagnosis. In various clinics the incidence of degeneration has been estimated to be between 3 and 10 per cent. This alone if for no other reason, would be more than enough to justify operation in all cases.

In addition to this a certain number of gastric ulcers are complicated by hemorrhage some patients dying without benefit of surgery some dying as the result of surgery and hemorrhage and some recovering in spite of surgery done at an inopportune time. A certain percentage of these ulcers perforate followed by an appreciable mortality regardless of the method of treatment. Some individuals having palliative emergency operation for hemorrhage or perforation will subsequently need to undergo a second operation for one of a variety of reasons.

The medical cure of gastric ulcer can never be counted upon and many individuals suffering from the disease go through life as semi-invalids who might otherwise be normal individuals if given the benefit of surgery.

The present method of procedure in many clinics is to treat all gastric ulcers initially medically for a period of time, usually several weeks. If healing is thought to be taking place by remission of the patient's symptoms, by x ray and gastroscopic examination and by disappearance of occult blood in the stool, the regime is continued. That this method of deduction may too often be entirely fallacious has been the experience of many observers. The *bad* sequence of events may be as follows: symptoms and findings may improve regardless of the nature of the lesion and the doctor and the patient both feel assured that everything is progressing favorably. The patient subsequently has a return of symptoms but is not particularly disturbed until some months later when upon re-examination the lesion is undoubtedly malignant and frequently not responsive to any type of therapy. This sequence of events occurs too frequently to make the medical treatment of gastric ulcer a safe procedure.

In the light of the safety of modern surgery, the result of many new discoveries which are too well known to recount at this time, re-evaluation of medical versus surgical treatment of many lesions is long overdue. Gastric ulcer is an outstanding example.

The mortality of subtotal gastric resection for gastric ulcer in experienced hands is unbelievably small, considerably less than that for duodenal ulcer because the duodenal stump is away from the lesion and its adequate involution without damage to the common duct is easily accomplished. Jejunal ulcer the bane of surgery for duodenal ulcer for all practical purposes does not occur following gastric resection for gastric ulcer. The postoperative course and subsequent complete relief of symptoms are with few exceptions most satisfactory.

In the whole realm of surgery there are few more disappointing chapters than that associated with the therapy for cancer of the stomach. If cure is ever to be expected in any appreciable percentage of cases, it will be in those individual cases where the diagnosis is only made by the microscope and never where the gross appearance is self-evident.

Briefly then, surgery is indicated for all gastric ulcers because

1. There is no method of differentiation between benign gastric ulcers and ulcers showing early malignancy.

Because of their complications, namely hemorrhage and perforation.

3. Because there is no sure permanent medical cure for gastric ulcer.

4. Because of the safety of gastric resection and subsequent satisfactory result to the patient.

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# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## CLINICAL INVESTIGATION AND EVALUATION OF FOUR HUNDRED SIXTEEN CASES CONSECUTIVELY OPERATED UPON FOR PEPTIC ULCER

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### INTRODUCTION

PEPTIC ulcer is primarily a medical disease. Surgery has a place in its treatment only when complications develop. In the past surgical procedures were done on an empirical basis. The results of this surgery have proved unsatisfactory.

The relationship between excessive acid and the occurrence of peptic ulcer has been emphasized through experimental and clinical work of Wangensteen and associates, Matthews and Dragstedt, Mann and Williamson, and others. They have shown that no longer is an empirical approach necessary to the problem of peptic ulcer but it can now be approached scientifically on the basis that the most important single factor in the prevention of recurrence is the control of acid secretion by the stomach.

Most of the controversy today is with regard to the surgical procedure which will best accomplish the purpose of abolishing or greatly diminishing acid secretion.

It is now generally agreed that subtotal gastric resection is the most satisfactory surgical treatment for peptic ulcer. Partial gastrectomy has attained its present position only in the last twenty to twenty-five years in this country. Prior to this time various and ingenious operations had been devised in an attempt to attain a satisfactory cure for peptic ulcer. Gastrojejunostomy, excision of the ulcer, operations on the pylorus, gastroduodenostomy, the Devine and Von Fraenkel's pylorus operations, as well as Cohnell fundussectomy and combinations of these procedures had been attempted. Each of these operations had its staunch advocates who presented seemingly sound argument for their choice. Notwithstanding the sincere enthusiasm of the early pioneers in surgery the operative procedures then so vigorously defended had no real firm physiologic foundation which could endure.

The popularity of gastrojejunostomy in the treatment of duodenal ulcer was based mainly on the supposed high incidence of good results, technical ease of performance and the low mortality. Unfortunately, however, many

bridgement of thesis toward M.D. partial requirement of M.D. degree in Surgery Dec 14 1917 University of Minnesota Medical School

failed to receive relief from this procedure either because of persistence of ulcer or because of the occurrence of gastrojejunal ulcer.

The incidence of recurrent ulcer following gastrojejunostomy has been reported as varying from 3 to 30 per cent. St. John reported 6.8 per cent marginal ulcer following gastrojejunostomy. Balfour 4 per cent recurrent ulcer and 9 per cent postoperative hemorrhage. Berg<sup>1</sup> noted incidence of 30 per cent recurrence. Walters,<sup>2</sup> 3 per cent. Marshall and Klef<sup>3</sup> 24 per cent. Lahey 6 per cent; and Church and Hinton, 23.8 per cent.

European surgeons had already discarded gastrojejunostomy and were employing subtotal gastric resection. Gradually the value of subtotal gastric resection began to be appreciated in this country. Hinton,<sup>4</sup> reported that he had been doing subtotal gastrectomy for peptic ulcer since 1931. Walters and associates<sup>2</sup> reported that in 1940 gastrojejunostomy constituted 50 per cent of operations for duodenal ulcer at the Mayo Clinic and gastrectomy slightly more than 40 per cent. In 1943 this was reversed with gastrectomy being done in over 57 per cent and a decrease of gastrojejunostomy to 41 per cent. Counseller and associates<sup>5</sup> reported that in 1944 at the Mayo Clinic, gastrectomy was done in 62 per cent of the cases and gastrojejunostomy in 37 per cent. Marshall<sup>3</sup> at the Lahey<sup>6</sup> reported that in 393 cases of peptic ulcer 318 patients had subtotal gastric resections and 75 had gastrojejunostomies done. Sanders<sup>7</sup> reported that in 1940 subtotal gastric resection was done in 50 per cent of the cases, and in 1945 in 71 per cent of the cases.

With the acceptance of subtotal gastric resection, considerable difference of opinion arose as to the technique. The main differences concern themselves with the extent of the resection, the length of the proximal or afferent duodenal jejunal loop, and extension of the duodenal ulcer.

The following surgeons have been ardent proponents of extensive gastric resection for ulcer: Finsterer and Cunha,<sup>8</sup> Lewinsohn,<sup>9</sup> Berg, Lahey and Marshall, Allen and Welch, Steinberg<sup>10</sup> and Wangensteen and Lamm.<sup>11</sup>

Advocates of the smaller gastric resection are Ruenhoff,<sup>12</sup> Hunt,<sup>13</sup> Sanders,<sup>14</sup> Holman and McSwain,<sup>15</sup> Strauss and associates,<sup>16</sup> and Hener and Holman.<sup>17</sup> These men favor the smaller resection because they believe reoperation is less difficult in the event of a recurrent ulcer. They further believe that extensive resection results in unfavorable postoperative symptoms, and that sacrificing so great an amount of stomach will not proportionately increase the degree of achlorhydria or lessen the number of recurrences.

The length of the afferent loop has also been the subject of much discussion. Lahey<sup>6</sup> has been an advocate of the employment of a long proximal loop. He based his contention on the following items: (a) alkaline jejunal contents are lumped in the residual gastric pouch and aid in lowering gastric acidity; (b) residual gastric pouch empties better; (c) possibility of postoperative obstruction of proximal loop is lessened; (d) reoperation is made easier when stomal ulcer occurs.

Wangensteen<sup>11</sup> has emphasized the importance of utilizing a short afferent proximal duodenojejunal loop in the gastrojejunal anastomosis in the Billroth

II pattern. He based his views on clinical and laboratory data. He stressed the importance of the secretin factor: partial separation and probability of increased susceptibility of unusually lower segments of the small intestine to injury by acid gastric secretions. Merendino and coworkers<sup>14</sup> reported that extensive gastric resection (75 per cent) in dogs when accompanied by a long afferent duodenojejunal loop was followed by a high incidence of spontaneous gastrojejunal ulcer. When histamine in beeswax was administered to such dogs, stomal ulcer occurred regularly. When gastrointestinal continuity was re-established by a short afferent duodenal loop in the Billroth II plan of operation, stomal ulcer after extensive gastric resection could not be provoked even when histamine in beeswax was administered. Mason and Grossman<sup>15</sup> stated that the more distal the loop of jejunum which was used for gastrojejunal anastomosis the more likely is jejunal ulceration to occur. Kiefer<sup>16</sup> reporting the result of gastric resection at the Lahey Clinic noted a recurrence rate of 11.4 per cent following gastric resection of duodenal ulcer in cases where the long proximal loop was employed. Lewisohn<sup>17</sup> in a recent article took issue with those who perform subtotal gastric resection for ulcer and leave the duodenal ulcer in situ. He contended that removal of the ulcer is a necessary part of the operative procedure. He stated that the line of resection should be below the ulcer. He felt that leaving an intact pyloric antrum, even if the antral mucosa is removed, is not a satisfactory practice. This opinion is shared by Lahey, Hinton and Sanders.

On the contrary some surgeons (Steinberg<sup>18</sup>, Magee, Colp and associates,<sup>19</sup> Wolfson and Rothenberg<sup>20</sup> and Wilson<sup>21</sup>) did not believe it necessary to remove the duodenal ulcer itself to prevent recurrent ulcer after extensive gastric resection.

The success or failure of operative procedures for ulcer in the past has been evaluated mainly on the basis of recurrent ulceration. There have been few comprehensive follow-up studies which completely evaluated the functional end results. In a recent comprehensive study of 193 patients in whom resection was done for duodenal ulcers, Allen and Wilb<sup>22</sup> reported the result in the 129 patients on whom follow-up studies were done. The overall mortality was 51 per cent, with a elective mortality of 36 per cent. Sixty-nine per cent of the patients were graded as excellent. These patients were entirely asymptomatic. An additional 18 per cent had trivial symptoms such as intolerance to a fatty meal or a rare attack of indigestion after a heavy meal and were also included in the excellent result. The patients listed satisfactory complication 6 per cent of the group and were those who were improved by the operation but still had symptoms requiring medical care or special diet. Definitely poor results occurred in about 7 per cent of the group. The poor results consisted of three cases of recurrent ulcers, 7 per cent, three cases of postoperative hemorrhage without evidence of ulcer, 7 per cent, and three cases of severe postresection symptoms, 3 per cent.

Rienhoff<sup>23</sup> in a recent paper advocated the return to a conservative gastric resection for duodenal ulcer. In follow-up study of 460 patients operated

upon, he found it necessary to subject 29 of the 255 who survived the operation to re-operation for recurrent ulcer an incidence of 11.3 per cent. Hemorrhage occurred postoperatively in 96 or 10 per cent of the follow-up cases in addition, 4 patients, or 1.6 per cent complained of pain. He reported a 2 per cent mortality in the series.

Miller<sup>27</sup> in reporting results of 230 resections for peptic ulcer noted mortality of .8 per cent for elective surgery. He stated that 90 per cent of the patients were cured and 10 per cent improved. No mention was made of recurrences.

McClure and Falls,<sup>28</sup> doing extensive gastric resection, reported a recurrence rate of 4 per cent and suspicion of recurrence in an additional 4 per cent. They stated that these recurrences occurred in patients who had had limited resections. Seventy-five per cent of their patients were reported as excellent or good results, 4.6 per cent as fair, 8.6 per cent as poor, and 5.6 per cent were not classified.

Walte and co-workers<sup>29</sup> reported 21 consecutive operations on a selected group of patients. Follow-up was carried out on 197 patients. The operative mortality was 1.9 per cent. 5 per cent developed anastomotic jejunal ulcers, 83.5 per cent of the patients were well without restriction of diet and 14 per cent required restrictions of diet or activity or both.

Sanders, who advocates a 50 to 60 per cent resection together with the excision of the duodenal ulcer, reported an incidence of recurrent ulcer of 8 per cent, and a mortality of 3 per cent.

Herg<sup>3</sup> reported six recurrences, 1.1 per cent in a series of 516 cases.

Dragstedt<sup>30</sup> has stimulated a renewed interest in vagotomy for the treatment of peptic ulcer. At the present time it is not possible to evaluate this procedure because of the recentness of its re-introduction in the therapy of peptic ulcer. It will be some years before vagotomy can be thoroughly evaluated. This operation is being given a first clinical trial by several competent investigators. In the meantime it is important that one maintain an open mind and neither hastily condemn or hastily praise the procedure.

#### DESCRIPTION OF PROGRAM

The present study was conducted to survey and evaluate results of the surgical procedures in the treatment of peptic ulcers at the University of Minnesota Hospitals from Jan. 1, 1940, to July 1, 1945.

Four-hundred sixteen patients consecutively operated upon for peptic ulcer were considered in this investigation. All were followed by questionnaire to the patient, and by clinical examination in the outpatient department.

Since 1910, this clinic has met each morning each week for patients who have had, or will have, gastrointestinal surgery. These patients are seen by the Chief of the Department of Surgery and members of his staff interested in the problem of peptic ulcer. An attempt is made to maintain complete follow-up of the patient's status postoperatively by having the patient report to the clinic one week following discharge from the hospital, then one month later;

then at three-month interval for a period of one year. During the second year following the operation the patient reports every six months. Following the second year he is examined once a year thereafter. If the patient does not report for checkup, periodic letters are sent to him, urging his return for examination. In the event he is unable to do so a written report of his present health is requested. The results of these periodic visits and the information obtained by the questionnaires form the basis of this report.

### QUESTIONNAIRE

NAME \_\_\_\_\_

TELEPHONE \_\_\_\_\_

HOSPITAL \_\_\_\_\_

We are interested in knowing how your digestion since our operation for ulcer. We would appreciate your answers to the following questions. You may write our answers to the questions in the space provided below for each question. If the space provided is not sufficient you may use the back of this letter.

- How is your general health at the present time?  
Good or otherwise Explain.  
Are you free from pain?  
If so you found blood in the stool? If so you had tarry stools?  
Has there been any vomiting?  
Are you having any difficulty with your digestion?  
List any specific complaints.
- Have you gained, remained the same or lost weight?  
Give amounts and period of time.  
What is your height?  
What is your present weight?
- Are you able to eat 3 regular full meals a day? Give an example of average meal for each period of the day.
- Are you able to eat all foods?  
List any and all foods which you feel give you trouble.
- Do you drink milk? Did you drink milk before operation?  
Are you able to work? What type of work do you do?  
How soon did you return to work after operation? We should like to know about our periodic checkups in the future. A self-addressed envelope enclosed for our convenience in returning this questionnaire.

In evaluating results of subtotal gastric resections in these cases, the following aims of any surgical procedure were considered: (1) to relieve the patient of the disease (2) to restore him to a state of health as normal as possible (3) to not unduly endanger the life of the patient (4) not to produce a result involving more serious implication than the original disease for which the patient was treated.

The investigation and evaluation covered the state of health of the patient postoperatively presence or absence of symptoms for which he was operated upon, occurrence of new symptoms more serious than the original condition and qualitative food intake, digestive function, ability to maintain normal nutrition ability to carry on normal occupations, and the patient's own evaluation of the result of the operation.



## OPERATIVE PROCEDURE

In 1938 and 1940 this clinic began a search for an operation which would deal satisfactorily with the ulcer problem. Lamm reported findings of laboratory investigation. In 1940 the clinical phase of the program was begun and three types of operation were performed for duodenal ulcer namely Groups III, IV and IV A. The Group IV was discontinued because results indicated it was an unsatisfactory operation. Since 1941 the standard procedures have been Groups III and IV A.

Group III operation consists of at least 75 per cent resection, followed by a retrocolic anastomosis with the jejunum at the duodenojejunal junction producing a short afferent loop with inversion of the lesser curvature in the Hofmeister pattern.

Group IV A differs from Group III only in the handling of the duodenum. In this instance the pyloric antrum is sectioned about two to three finger breadth proximal to the pyloric sphincter and the anti reflux mucosa is covered employing the pyloric sphincter and the antral musculature for closure. The Group IV A procedure is utilized only in those cases of the so-called difficult or irreparable duodenal ulcer.

Group IV differs from the IV A operation in that the antial mucosa is left intact. Operative Groups III, IV and IV A are illustrated in Fig. 1.

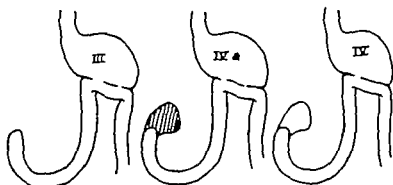


Fig. 1.—Surgical procedures (Groups III, IV and IV A) in the treatment of peptic ulcer.

## CLINICAL OBSERVATIONS

In an diagnosis of peptic ulcer duodenal ulcer should be considered part from the gastric ulcer. The duodenal ulcer represents a different problem. There is always the possibility that malignancy is present in the gastric ulcer. Prolonged observation and medical therapy may unfavorably affect the outcome of the patient with a gastric lesion by delaying surgery until the lesion has become inoperable from a curative standpoint. Although typical lesions of benign ulcer or carcinoma are not difficult to diagnose there are many instances where

despite all diagnostic aids, it is not always possible to make a definite diagnosis until the permanent microscopic section are interpreted. Wangensteen noted many reversals of diagnoses whether made by clinician, radiologist, gastroscopist, surgeon at operation or pathologist. A more critical attitude toward gastric ulcer should be adopted so that patients will be referred by the internist for resection at an earlier date. Certainly questionable lesions should be given three to four weeks medical management to determine whether or not healing will occur. Even if healing does occur some lesions will turn out to be carcinomatous.

In the duodenal ulcer medical management should be carried out for an extended period of time since the majority of patients can be adequately controlled. It is only in cases where medical management has proved ineffective that surgery should be undertaken.

The 416 cases therefore were divided into two series. Series I consisted of those cases in which the problem was that of duodenal ulcer and Series II were those with ulcerations on the gastric side of the pylorus.

#### LOCATION OF ULCER

In the 416 cases of peptic ulcers followed, 203 cases, or 61 per cent, were duodenal. 13 patients were male and 40 female a ratio of 5 to 1. Gastric lesions totaled 90 cases, or 21.5 per cent. 72 males and 18 females, a ratio of 4 to 1. The remaining 3 cases or 17.5 per cent consisted of duodenal and gastric lesions, duodenal and gastrojejunal occurring together and gastrojejunal lesions alone. In this group there were 58 males and 1 female. Complete totals revealed that males outnumbered females by a ratio of 4.6 to 1. The location of the ulcer according to sex is shown in Table I.

TABLE I LOCATION OF ULCER

	MALE	FEMALE
Duodenal	11	3
Duodenal and gastrojejunal	18	1
Duodenal and gastric	2	4
Gastrojejunal	15	4
Pyloric		
Gastric	7	1
Total cases 41	44	21

#### CASES WITH PREVIOUS SURGERY

Table II shows the number of cases in which previous surgery had been done. Forty patients, or 9.6 per cent had surgical repair of free perforations. Forty had gastroenterostomies. 8 patients had small resections and one patient had the Devine pylorus operation. Two had total removal of ulcer. In some instances, multiple operative procedures had been done on the same patient.

#### INDICATIONS FOR SURGERY

Indications for gastric resections were intractable pain, hematemesis and obstruction. Intractable pain was the single indication. 83 of the 416

TABLE II. CASES WITH PROVEN ACIDITY

LOCATION OF ULCER	TOTAL NO. OF CASES	SURGICAL REPAIR OF PERFORATION	GASTROCYTOMY	SMALL RESECTION	OTHER
Duodenal	23	2	10		
Pyloric		1			
Gastric	81	3	2		
Duodenal and gastropyloric	18	4	15		
Duodenal and gastric	26	1	1		
Gastropyloric	19	3	1	6	1 Duodenal ex-cision 3 Local ex-cision alone
Total	1	4	4		3

No evidence of gastric ulcer at the time of surgery and examination by pathologist.

cases, or 70 per cent of the patients who were operated upon for ulcer in this clinic. These patients were unable to control the pain under medical treatment. Pain occurred in combination with other symptoms in 318, or 76 per cent of the cases.

*Acute massive hemorrhage* which endangers life, constitutes a major problem in the handling of the ulcer patient. Whether bleeding will stop or continue is always questionable. In the younger individual bleeding usually will cease spontaneously under conservative therapy. However, there were in the study five patients under the age of 45 years whose bleeding persisted. The youngest of these was a 14-year-old boy who finally needed emergency surgery. The decision to operate for a life-threatening hemorrhage in the patient over 45 years demands careful consideration of all findings in the individual patient. Age and the degree of arteriosclerosis appeared to be important factors in the mortality of the older age group. Twenty-six patients were admitted because of acute massive hemorrhage. Of this group 22 underwent emergency surgery with ensuing mortality of 7 or 31 per cent. The youngest fatality was 39 years of age while all others were over 50 years. Massive hemorrhage occurred in all cases. Six patients had bled to low levels with associated drops in blood pressure to shock levels. Despite repeated transfusions, hemorrhage continued with repeated drops in blood pressure to shock levels, indicating that a fairly large vessel was open in the base of the ulcer. At operation the patients with duodenal ulcer were bleeding from the gastroduodenal artery or one of its branches.

The longest period of hemorrhage prior to surgery was thirty-eight days and the shortest four. None of the patients were operated upon in the early course of their hemorrhage. Conservative therapy had been attempted, but had proved unsuccessful. Surgery was done as a last resort with the full realization that these patients were poor surgical risks.

The amount of blood transfused prior to surgery varied from 2,000 to 9,000 cc. Attempts to establish good preoperative hemoglobin levels were unsuccessful because the patients' blood loss continued to exceed the replacement.

Six patients died from unavoidable complications. One patient (MM) died on the first postoperative day from a massive hemorrhage due to erosion of a

duodenal ulcer hit the gastroduodenal artery. She had previously had a gastric resection for a bleeding gastric ulcer and the presence of a duodenal ulcer was not detected at surgery. The mortality in the group of patients who were operated upon as an emergency for a fatal hemorrhage is indicated in Table IV.

In 1° cases, or 9 per cent hemorrhage occurred without any other accompanying symptom, the patient having little or no warning of the onset. This constitutes a very important indication for surgery because of the difficulty of managing such an individual by conservative means. These patients should be operated upon to prevent future episodes.

History of hemorrhage associated with pain was given in 104 cases, or 43 per cent. 7 or 13 per cent had hemorrhage, pain and vomiting and 43 or 103 per cent, had hemorrhage, pain, and obstruction.

Hemorrhage occurred as a symptom in 51.6 per cent of the cases.

Obstruction as the only symptom was found in 3 cases. When associated with severe pain, it was found to be present in 4 cases or 11.9 per cent. Obstruction, pain, and hemorrhage occurred in 43 cases, or 103 per cent.

The indications for surgery are shown in Table III.

TABLE III. INDICATIONS OF SURGERY

	GROUP I		GROUP II	
	NUMBER	PER CENT	NUMBER	PER CENT
Pain	5	19.9	20	50
Hemorrhage	9 (3)	27	8 (1)	33
Obstruction	3	9.9		
Pain and hemorrhage	77 (10)	53.6	47 (4)	30.0
Pain and vomiting	4	14.1	19	11
Pain and obstruction	41	14.5	6	6.6
Pain, vomiting and hemorrhage	47 (3)	14.1	10 ( )	11.1
Pain, hemorrhage and obstruction	19 (3)	11.6	5	5.5
	126 (19)*		60 (7)*	

\*Twenty-six patients died of hemorrhage. Of 194 patients who were operated upon, 168 patients died of hemorrhage, of which twenty-six patients died.

## MORTALITY

The over-all mortality in the 416 patients operated upon was 19 patients or 4.3 per cent. This includes the seven cases described in Table IV of emergency operations for acute hemorrhage. Twelve deaths, 9 per cent, occurred as a result of elective procedures. Eight cases were classed as unavoidable deaths, and 4 were related to surgical complication. These operations were done by 4 surgeons and 6 surgical residents. The immediate mortalities of elective operations are described in Table V.

TABLE IV. A

	NUMBER OF CASES	NUMBER OF DEATHS	PERCENTAGE
Elective surgery	241	12	5
Emergency surgery	22	7	31.8
Over all	41	19	4.3

In response to question  
leaving the hospital. The cr  
VI From the information

TABLE IV MORTALITY OF EMERGENCY CASES OF ACUTE HEMORRHAGE

BOAT NO. AGE, SEX, A B KEY	DIAGNOSIS	ADMISSION IN (M.)	WOUND OF BLEED IN (DAY)	PRE OP IN. (X)	OPERATION AND TE	AMT BLOOD TRANS- FUSED PRIME (C.C.)	CAUSE OF DEATH (POST MORTEM)
429 (A.C.) (m)	Duodenal	76	4	581	Group III (4/11/41) Pos- terior wall duo- denal ulcer ligh- tly gastro- duodenal artery	3000	Died on O.R. at onset of opera- tion rheumatic heart disease with regurgitation, lea- sion and mitral valvulitis, pulmo- nary edema
193 (E.D.) (m)	Duodenal	65	8	9	Group III (8/27/41) Pos- terior wall duo- denal ulcer ligh- tly gastro- duodenal artery	6750	8th P.O. day renal arteriosclerosis with aneurysm, pul- monary embolism localized pancrea- titis with fat in crossed pancreas
234 (K.D.) (m)	Duodenal	82	11	11.0	Group III (7/14/43) Bled tag from gastro- duodenal artery ligated proximally and distally ulcer perforated into pancreas	2750	4th P.O. day acute pancreatitis with necrotic area in head of pancreas peritonitis, pul- monary abscess tissue
000 (M.B.) (f)	Duodenal	77	9	9.75	Group III (2/1/44) Pos- terior duodenal wall ulcer ligh- tly branch gas- tro duodenal artery	3500 plus 1200 (plasma)	Immediately P.O. acute recurrent cardiomyopathy with mitral stenosis and myocardial necrosis thrombotic pericar- ditis bilateral pulmonary edema
057 (K.P.) (m)	Gastric	45	10	9.7	Group III (4/7/44) ulcer on lesser curva- ture	8000	11th P.O. day hemorrhage from pulmonary arteries septo- cardiac, right and left heart failure
7824 (M.M.) (f)	Gastric and duodenal	84	16	6.7	Group III (11/3/44) Bled tag gastric ulcer	2400	2 Day P.O. acute hemorrhage from erosion of duo- denal ulcer into gastro duodenal artery
2254 (J.J.) (m)	Gastric	106	30 in Lower Bump 8 in U of M. Hump	1.3	Group III (1/22/44) Bled tag pyloric ulcer	2450 (Also trans- fused 1 local hump)	15 H P.O. cere- bral thrombosis cerebral arterio- sclerosis 1st cerebral embolism

for ulcer. Fifteen patients were lost for follow up. Every attempt to contact these patients had been made without success.

## AGE INCIDENCE

The average age of the patients in Series I was found to be 45.8 years. The youngest patient was a male who was operated upon at the age of 14 years for recurrent massive hemorrhage from a duodenal ulcer which began at 10 years of age. The oldest patient was a man, aged 65 years.

In Series II the average age was 34.3 years. The youngest patient was 13 years, and the oldest, a man, 65 years. Table VII indicates the age distribution according to sex and age period for Series I and II.

TABLE V. INHENT TO MORTALITY OF ELECTIVE OPERATIONS

PATIENT NO.	AGE (YR.)	SEX	INDICATION	OPERATION	DATE	CAUSE OF DEATH
W455	37	f	Duodenal	Group IV	2/19/40	Postoperative septicemia, bases of liver abscesses, inversion of common bile duct into pylorus, distention of proximal loop between ligament of Treitz and anastomosis
W324	71	f	Gastric	Group III	10/14/40	Pulmonary embolus
W412	37	f	Duodenal	Group III	4/2/41	Blood transfusion reaction with anuria and uremia
W323	34	m	Duodenal	Group III	8/5/41	Perforation of duodenal stump with peritonitis, bronchopneumonia and pulmonary abscess
W124	0	m	Benign pyloric	Group III	11/19/41	Acute pancreatic necrosis of unknown etiology, anastomosis was in good order
W4613	8	m	Duodenal and gastric	Group III	12/17/41	Pneumonia
W330	4	m	Gastrojejunal	Group III	9/25/41	Generalized peritonitis, leakage of suture line, colon, and gastrojejunal anastomosis
W334	37	m	Gastric	Group III	11/15/43	Died during surgery, shock of hyperthermia, temp 107° F. At post mortem examination, pulmonary atelectasis, edema, cysts of pituitary, chronic passive congestion liver and spleen, renal and cerebral arteriosclerosis
W421	44	m	Duodenal	Group III	11/18/41	Subarachnoid hemorrhage, small cerebral aneurysm and cerebral arteriosclerosis
W371	40	m	Duodenal	Group III	6/10/43	Severe coronary arteriosclerosis with multiple coronary thromboses
W448	60	f	Duodenal	Group III	8/7/44	Pulmonary embolus
W315	65	m	Duodenal	Group III	2/1/45	Duodenal fistula, right and left subphrenic abscesses, peritonitis, ruptured gall bladder

TABLE VI LATE MORTALITIES

HOSPITAL NO.	SEX	AGE (YR.)	RACE	DIAGNOSIS	OPERATION	DATE	LESS OF DEATH	AGE (YR.)
<i>Series I</i>								
741809	O.C.	60	m	Duodenal	Group III	7/17/41	Coronary thrombosis, myocardial infarction	31
684321	P.P.	74	m	Duodenal	Group III	3/7/42	Unknown (Reported well until death)	11/
735061	A.L.	59	m	Duodenal	Group IVA	3/25/45	Pyelonephritis with abscess	11/
657618	E.M.	85	m	Duodenal	Group IV	7/30/40	Cardiac death; mitral stenosis with cardiac decompensation	3/
746107	P.D.	63	m	Duodenal	Group III	7/27/41	Palmonary hemorrhage	11/3
747007	E.M.	62	f	Duodenal	Group III	4/17/41	Coronary thrombosis	4/3
703200	O.H.	65	m	Duodenal	Group IVA	7/23/41	Cerebral hemorrhage	1/2
730923	M.B.	22	f	Duodenal	Group III	2/21/41	Coronary thrombosis	8/
<i>Series II</i>								
643245	H.C.	51	m	Duodenal and gastric	Group III	12/11/40	Nephritis	4/28
<i>Series III</i>								
656130	M.H.	36	f	Pyloric	Group III	5/20/40	Lymphosarcoma of neck with metastases to mediastinal nodes	7/5
735239	H.W.	52	m	Gastric	Group III	6/13/43	Pulmonary tuberculosis	8/29
604023	B.H.	59	f	Pyloric and gastric	Group III	8/13/40	Metastases from carcinoma of cervix	9/10
637023	W.F.	71	m	Gastric	Group III	8/31/43	Metastases from carcinoma of hip	8/20
725333	M.O.	64	f	Gastric	Group III	8/17/43	Coronary thrombosis	8/29
703948	V.O.	29	m	Gastric	Group III	1/3/41	Bulbar polio encephalitis	9/2
749100	W.W.	61	m	Pyloric	Group III	1/17/43	Accidental death	8/21
641266	A.H.	46	f	Gastric	Group III	10/9/40	Pneumonia	8/7
691261	J.A.	73	m	Gastric	Group III	3/19/41	Cerebral hemorrhage	1/1

## DURATION OF SYMPTOMS

Since duodenal ulcer is a chronic recurrent disease symptoms very often occur over a long period of time. In Series I the average duration of symptoms was found to be 19 years. One patient (O.D. No. 653622) with a duodenal ulcer was encountered whose symptoms extended over a 65-year period, during which time he was periodically troubled with epigastric distress. Ten years prior to operation he was forced to remain on a Rippy diet continuously because of severity of the pain. In 1943, he was admitted for an acute perforation of a duodenal ulcer but at that time refused surgery. Later a subphrenic abscess was drained. On June 26, 1944, a subtotal gastric resection was done.

TABLE VII AGE DISTRIBUTION

AGE ( )	M	F	MALE
10-20			6
21-30	10		
31-40	74		31
41-50	76		19
51-60	64		17
61-70	2		6
71-80	6		2
81			1
	171		83
	Average age 45		Average age 41
	Youngest age 14		Youngest age 10
	Oldest age 85		Oldest age 71
	New 11		
10-20			0
21-30			0
31-40	8		
41-50	70		
51-60	19		4
61-70	17		5
71-80	3		1
81	0		0
	117		13
	Average age 50.8		Average age 63.5
	Youngest age 1		Youngest age 36
	Oldest age 75		Oldest age 71

and he has had no difficulty since except for a volvulus of the cecum, which was operated upon. The patient is now 87 years of age and feeling well.

In Series II the average duration of symptoms was found to be 8.4 years. The shortest period of vomiting in this group was one week. This occurred in a 56-year-old woman (9P N 46286) who was admitted because of massive gastrointestinal hemorrhage. She had had no previous difficulty prior to this time and was operated upon as an emergency. A small benign gastric ulcer on the lesser curvature was found to be the source of the hemorrhage. The longest period of difficulty encountered in this series was 37 years.

#### EXTENT OF GASTRIC RESECTIONS

In 1940, the extent of the resection was determined by measurement in square centimeters. Subsequently this method of determining the amount of resection was discarded in favor of the actual weight of the specimen. It was believed that a more accurate determination could thus be accomplished. The stomach specimen was weighed after excision of all attached tissues including omentum and fatty tissues.

In Series I the average weight of the resected specimen in the nonobstructed patients was 180.23 Gm. The average weight in the obstructed patients was found to be considerably higher, namely 461.14 Gm.

The surgeon must give careful consideration to the fact that the stomach of the obstructed patient is larger and he must therefore remove a correspondingly large amount in order to attain a 75 per cent resection.



TABLE VI. LATE MORTALITIES

HOSPITAL NO.	NAME	AGE (YR.)	SEX	DIAGNOSIS	OPERATION	DATE	CAUSE OF DEATH	DATE OF DEATH
<i>Series I</i>								
741504	C. C.	60	m	Duodenal	Group III	7/17/41	Coronary thrombosis, arteriosclerosis	8/2/41
604321	P. P.	74	m	Duodenal	Group III	3/20/43	Lakeview (Reported well until death)	1946
757561	A. L.	83	m	Duodenal	Group IV A	3/23/45	Pyelonephritis with uremia	11/1/45
637618	E. M.	59	m	Duodenal	Group IV	7/20/40	Cardiac death; mitral stenosis with cardiac decompensation	8/4/40
746167	F. D.	63	m	Duodenal	Group III	7/27/44	Palmonary hemorrhage	11/2/44
743007	E. M.	61	f	Duodenal	Group III	4/17/44	Coronary thrombosis	4/30/44
703700	C. K.	69	m	Duodenal	Group IV A	3/22/41	Cerebral hemorrhage	4/11/41
736932	M. R.	21	f	Duodenal	Group III	3/14/44	Coronary thrombosis	6/2/45
<i>Series II</i>								
643343	W. O.	31	m	Duodenal and gastric	Group III	11/31/40	Nephritis	1/4/41
<i>Series III</i>								
662556	M. R.	26	f	Pyloric	Group III	2/26/40	Lymphadenoma of neck with metastases to mediastinal nodes	7/4/40
753279	H. W.	50	m	Gastric	Group III	6/15/43	Palmonary tuberculosis	9/29/43
605023	A. H.	50	f	Pyloric and gastric	Group III	6/13/40	Metastases from carcinoma of cervix	9/13/40
637023	W. P.	71	m	Gastric	Group III	8/21/43	Metastases from carcinoma of lip	9/4/43
722333	M. G.	60	f	Gastric	Group III	8/17/41	Coronary thrombosis	1/29/42
703918	V. C.	29	m	Gastric	Group III	1/5/44	Bulbar palsy	1/2/44
723144	H. W.	1	m	Pyloric	Group III	4/17/43	Accidental death	6/21/44
681700	A. B.	46	f	Gastric	Group III	10/9/40	Stroke	6/7/41
691811	J. A.	73	m	Gastric	Group III	3/19/41	Cerebral hemorrhage	4/1/41

## DURATION OF SYMPTOMS

Since duodenal ulcer is a chronic recurrent disease symptoms very often occur over a long period of time. In Series I the average duration of symptoms was found to be 1.9 years. One patient (H. D. N. 663822) with duodenal ulcer was encountered whose symptoms extended over a 61-year period during which time he was periodically troubled with epigastric distress. Twelve years prior to operation he was forced to remain on a liquid diet continuously because of severity of the pain. In 1941, he was admitted for an acute perforation of a duodenal ulcer but at that time refused surgery. Later subphrenic abscess was drained. On June 26, 1944, a subtotal gastric resection was done.

TABLE IX. POSTOPERATIVE ACID DETERMINATION WITH TRIPLE II METHOD

	ACHLORHYDRIC	110 DEGREES	11-90 DEGREES	21-30 DEGREES	31 DEGREES PLUS
Series I (Duodenal Ulcer Gastrojejunal Ulcer etc.)					
MALES					
Group III	20		4	3	
Group IV	4				1
Group IVA	4	1		1	1
Total	28	1	4	4	1
FEMALES					
Group III	20			1	1
Group IV	1		1		
Group IVA	4				
Total	25		1	1	1
Total Male and Female	53	1		5	2
Total Determinations	179				
Series II (Gastric and Pyloric Ulcer)					
MALES					
Group III	4	1			
FEMALES					
Group III	8	1			
Total	12	2			
Total Determinations	30				

In the Group III operation, achlorhydria was found 85.6 per cent of the patients in Series I and in 88 per cent in Series II.

The result of the postoperative acid determinations indicated that achlorhydria was more easily obtained in female patients in the Group III operation. In Series I achlorhydria was found to be present in 90.9 per cent of the females as compared to 84.6 per cent in the males. No appreciable difference was noted in gastric ulcers (Series II) according to sex. Percentages for this group were as follows: males, 87.8 per cent; females, 88.8 per cent.

In the Group IVA operation, achlorhydria was found in 84.8 per cent of the patients in Series I. Determinations in this operation also show achlorhydria more easily obtained in females. It was found to be 100 per cent for the females and 82.7 for the males.

The combined result of Groups III and IVA in Series I shows 85.4 per cent achlorhydria in all patients. Results further indicated that 4 per cent of the patients exhibited acid of 31 degrees or over. In Series II no patient had acid determinations over 26 degrees.

In the Group IV operation there were 1 per cent of the patients with achlorhydria found in Series I.

#### EVALUATION OF PRESENT STATUS OF 416 PATIENTS CONSECUTIVELY OPERATED UPON

Many factors were taken into consideration in evaluating the patient as to their present status of health. Each patient was questioned regarding his opinion as to how he was feeling, symptoms he might be relating to digestion, such as pain, vomiting, hemorrhage and food intolerance, weight changes, and ability to work. Patients who stated that they had any difficulty

In Series II, the average weight of the specimen in the nonobstructed patients was 407.3 Gm. as compared to 46.4 Gm. in the obstructed.

The average weights of the resected specimens in the female patients who were not obstructed were significantly smaller than in the males in the cases of duodenal and gastric ulcer. In the obstructed patients, this relationship was not uniformly seen in all the series.

Table VIII indicates the average weights of the resected specimens as to whether patients were obstructed or not and according to sex.

TABLE VIII. WEIGHTS OF RESECTED SPECIMENS

NO. OF CASES		AVERAGE WT. RESECTED SPEC. (Gm.)	MINIMUM WT. RESECTED SPEC. (Gm.)	MAXIMUM WT. RESECTED SPEC. (Gm.)
MALES				
Obstructed				398
Nonobstructed				434
FEMALES				
Obstructed				123
Nonobstructed				158.91
NO. OF CASES		AVERAGE WT. RESECTED SPEC. (Gm.)	MINIMUM WT. RESECTED SPEC. (Gm.)	MAXIMUM WT. RESECTED SPEC. (Gm.)
MALES				
Obstructed		407.3	11.5	398
Nonobstructed		407.3	11.5	434
FEMALES				
Obstructed		46.4	11.5	123
Nonobstructed		407.3	11.5	158.91

#### GASTRIC ANALYSES

*Intraoperative Gastric Analysis*—Preoperative gastric analyses were done as a routine procedure in this study. Gastric acidity was determined in the morning. Breakfast was withheld from all patients. A No. 14 duodenal tube with four perforation at the tip was introduced through the nose into the stomach and continuous suction was employed. Fasting specimens were obtained and 5 mg. of histamine (0.5 mg. histamine base) were given in three consecutive doses at one-half hour intervals to provide the stimulus for gastric secretion. Gastric acidity was determined by the usual colorimetric titration, using Thymolphthalein as the end point for free hydrochloric acid and phenolphthalein as the end point for the total acid. The maximum determination of the three periods was taken, and the average value of 71.5 degrees of free acid was found in Series I and in Series II 49.7 degrees.

*Postoperative Gastric Analysis*—Postoperative acid determinations were made in the same manner as described in preoperative gastric analyses. Table IX shows the postoperative values obtained in the two series according to sex and type of operation. A total of 339 patients had one or more determinations done. These patients were all tested with triple histamine; all other cases were excluded.

indicated studies. All other patient reported for regular periodic checkup examinations. The patient in the survey were evaluated on the basis of their statements in answer to the questionnaires, clinical observation and personal

TABLE V—CON'D

YEAR	MALE FEMALE	OPERATED UPON	LOST	DEATH WEEK LATE	FOLLO ED	FLI GOOD	SATIS	POOR
From 11 (Anterior and Pyloric Ul)								
7 Years Followed								
1942	M F Total	9 6 15	1 — 1	— 1 1	— 2 1	— — 1	6 1 7	1 1 1
1941	M F Total	14 0 14	— — 1	1 — 1	1 — 1	1 — 1	1 — 1	— — 1
8 Years Followed								
1941	M F Total	23 6 29	3 0 3	1 1 2	1 2 4	14 0 1	14 1 15	1 1 2
1940	M F Total	11 4 15	— 1 1	1 — 1	1 1 1	— 1 1	1 1 2	— — 1
5 Years Followed								
1941	M F Total	34 10 44	3 1 4	1 1 2	1 4 5	24 4 28	2 1 3	4 — 4
1940	M F Total	11 1 12	— — 1	— — 1	— 4 4	— 1 1	3 1 4	1 1 2
4 Years Followed								
1941	M F Total	46 14 60	1 1 2	1 1 2	1 4 5	18 1 19	2 4 6	8 3 11
1940	M F Total	10 — 10	— — 1	— — 1	1 — 1	4 — 4	2 — 2	1 — 1
3 Years Followed								
1941	M F Total	63 16 79	1 1 2	4 1 5	4 4 8	34 10 44	7 1 8	24 2 26
1940	M F Total	7 — 7	— — 1	— — 1	1 — 1	1 — 1	4 — 4	1 — 1
2 Years Followed								
1941	M F Total	72 18 90	3 1 4	4 1 5	5 4 9	60 1 61	4 1 5	14 7 21

were requested to return to the outpatient department at an appointed time for clinical observation which included x ray examination, hemoglobin, and other

TABLE XL RESULTS ACCORDING TO SEX

	SEX	OPERATED	DEATH	DEATH	DEATH	DEATH	DEATH	DEATH	DEATH	DEATH	DEATH
		TYPE	LOST	IMMED	LATE	FOLLOWED	KEYELL	WOOD	BATES	FOOT	
Series I Duod. and Ulcer Gastropyloric Ulcer											
7 Year Followed											
1911	M	44	4		2	36	7	19		7	3
	F	6		1		5	1	3			1
	Total	50	4	1	2	41	8	22		7	4
1911	M	39	2	3	4	29	3	23		1	
	F	12	1	1		10	2	7		1	
	Total	51	3	4	4	39	5	30		2	
8 Year Followed											
	M	1	6	0	4	68	12	41		10	3
	F	18	1	2		15	3	19		1	2
	Total	19	7	2	4	83	15	60		11	5
1912	M	33	1			24	3	13			2
	F	9				9	1	4		4	
	Total	42	1			33	4	17		4	2
9 Year Followed											
	M	177	7	7	4	157	17	76		1	6
	F	77	1	2		74	4	14		8	1
	Total	254	8	9	4	231	21	90		9	7
1913	M	46		1	1	42	11	27		3	3
	F	7				7		4		1	
	Total	53		1	1	49	11	31		4	3
10 Year Followed											
	M	179	9	8	3	157	28	107		19	7
	F	24	1	2		21	4	18		4	1
	Total	203	10	10	3	178	32	125		23	8
1914	M	49			1	45	13	14		8	3
	F	11		3		8	4	1		1	
	Total	60		3	1	53	17	15		9	3
11 Year Followed											
	M	39	9	8	8	205	43	127		27	9
	F	45	1	8		37	8	19		9	1
	Total	84	10	16	8	242	51	146		36	10
1915	M	43	1	1	1	40	4	14		7	3
Jan	F	10				10	4	3			1
July	Total	53	1	1	1	50	8	17		7	4
12 Year Followed											
	M	271	10	9	7	245	61	130		34	10
	F	83	1	3		80	13	22		11	3
	Total	354	11	12	7	325	74	152		45	13

In the poor group the percentage of results was approximately the same. Included in this evaluation was the Group IV operation which showed 10 poor cases in the males, and one in the female.

In Series II there were 12 cases followed. There were 60 males and 1 female with the results shown in Table X B.

TABLE X B. RESULTS. SERIES II. GASTRIC PYLOUS ULCER

RESULTS	MALES (60)		PERCENT	FEMALE	PERCENT
	NUMBER			NUMBER	
Excellent	8		13.3	1	8.3
Good	3		5.0	2	16.7
Satisfactory	12		20.0	3	25.0
Poor			33.3		
Total	60		100	12	100

With the exception of two poor cases in the males there was no appreciable difference of results as to result in the sexes in this series.

#### RESULTS ACCORDING TO OPERATION

Table XI shows the result according to type of operation and period of observation for years. In Series I there were 31 patients followed who had Group III 55 Group IV A and 6 had Group IV. In Series II there were 79 cases followed. All patients evaluated according to type of operation have been followed for at least two years, and some as long as seven years.

The total number of patients and the percentages are given in Table XI A for the results according to type of operation.

TABLE XI A. RESULTS. SERIES I. DUODENAL ULCER, GASTROJEJUNAL ULCER

RESULTS	(II)		(33)		(6)	
	NUMBER	PERCENT	NUMBER	PERCENT	NUMBER	PERCENT
Excellent	4	40.0	14	42.4	1	16.6
Good	14	10.0	30	54.5	1	16.6
Satisfactory	13	11.8	10	1	1	16
Poor	6	3.4	1	1.6	3	50.0
Total	21	100	33	100	6	100

In the patient who had Group III operation in Series I it was found that 8 per cent were doing very well. These patients were asymptomatic, observed no dietary restrictions, and were capable of carrying on regular employment.

Patients graded satisfactory totaled 14.7 per cent. They were all benefited by the operation and were enjoying full general health. None of the patients required medical care except for minor complaints such as bloating, diarrhea, or belching, and so forth. In some patients it more frequently and others complained of symptoms of the so-called dumping syndrome. These patients were found to be adjusted to this difficulty by decreasing the size of the meal, eating more frequently, and allowing a short rest period following meals. All patients with the exception of one were capable of pursuing their

interviews. The results of the cases studied were classified into four categories, namely excellent, good, satisfactory, and poor.

The excellent group comprised those patients who were entirely free of symptoms, ate regular diet as to quality and quantity, maintained normal nutritional status, and were engaged in regular employment.

The patients classified as good enjoyed the same state of health as the excellent group but were placed in this group by reason of their terminology as to how they were feeling.

The satisfactory group consisted of patients who stated they were doing well but had occasional minor complaints, such as nausea, diarrhea, a feeling of fullness, or heartburn. Some patients were unable to eat as large a meal as they did prior to surgery. Included in this group also were the patients who had some food intolerances and those who had mild symptoms of the so-called dumping syndrome. Each patient who listed a complaint was observed clinically and was personally interviewed. It was found that generally all patients in this group were doing well and were able to carry on their regular employment.

The patients placed in the poor group were those who either had recurrent ulcerations, symptoms suggestive of recurrent ulcerations, or who stated they were in poor health. Patients who stated they were in poor health revealed they had distress after meals, were restricted as to quantity and quality of food, were unable to maintain normal nutrition, and unable to work.

There were 416 patients operated upon, of which 19 were immediate mortalities, and 38 late. Fifteen patients were lost to follow-up.

#### RESULTS ACCORDING TO SEX

All the patients evaluated have had follow-ups for at least two years, some as long as seven years. Table X shows the result according to sex and the period of observation by years. In Series I there were 20 patients followed. There were 16 males and 47 females, with the result shown in Table X.

TABLE X. A. RESULTS		SERIES I, D. CASE		TOTAL (GASTROINTESTINAL ULCER)	
RESULT	(MALES) PER CENT	PER CENT	RESULT	(FEMALES) NUMBER	PER CENT
Excellent	81	51	Excellent	15	32
Good	15	41.3	Good	28	40.4
Satisfactory	34	12.9	Satisfactory	11	23.4
Poor	10	4	Poor	2	4.3
Total	140	100	Total	47	100

It was found that the males showed 82 per cent excellent and good results as compared with 77 per cent in the females.

In the satisfactory group the females showed this result in 34 per cent of the cases as compared with 13.8 per cent in the males. The results of the three previously mentioned categories indicate that the females had more minor complaints. All three categories include men and women who were doing well.

TABLE VI—CO T

YEAR	OPERATED	LOST	DEATH			FOLLOWED	EXCEL.	GOOD	5 YRS	POOR
			IMMED	LATE						
			1 Year Followed							
III	17	7	1	6	10	41	119	7	8	
IV	9	1	1	1	6	1	1	1	3	
IVA	4			1	44	9	no			
Total	30	8	3	8	56	51	140	26	11	
1943 Jan	40		1		39	7	2	7	3	
1943 July	17	1		1	11	3	4			
Total	57	1	1	1	50	1	6		3	
			1 Year Followed							
III	37	7	17	7	71	49	141	74	9	
IV		1	1	1	6	1	1	1	1	
IVA	40	1			53	14	70	10	1	
Total	77	9	19	9	120	64	212	85	11	
Series II Control and Pilot										
1940 III	1	1	1	1	10		7		1	
III	18	1	1	1	10		7		1	
1941 III	14		1	1	10	1	8	1		
III	20	1		1	no	1	15	1	1	
1942 III	13	1	1	1	1			2		
III	44	4	1	5	5	7	no	6	1	
1943 III	1	0	0		14	1		3	1	
III	no	4	1	7	46	4	no	11		
1944 III	1	0		1	18	4	11	3	0	
III	81	4	5	5	64	8	40	14		
1944 Jan	9	0	0	1	8	1	6	1	0	
1944 July										
Total	24	4	5	9	78	9	40	15		

13, 1944. History of hematemesis, melena, and epigastric pain. Hemorrhage occurred on five occasions prior to admission during the previous year. He was operated upon on May 15, 1944, at which time 75 per cent gastric resection was done. The weight of the resected specimen was 155 Gm. Operative findings: one gastroduodenal ulcer perforated out of the pylorus and active duodenal ulcer.

The patient was readmitted on Oct. 5, 1944, because of epigastric pain and hematemesis. Transfusion was given and he was treated conservatively.

The third admission was for acute onset of paroxysmal irregular fibrillation and hyperkalemia. At this time the ulcer symptom was well controlled by medical management. The patient's fourth admission on March 1, 1945, was for recurrence of epigastric pain and melena. He was treated conservatively.

He was readmitted for the fifth time because of persistence of epigastric pain and recurrent hemorrhages. X-ray examination showed presence of stomach ulcer. The patient



TABLE VI RESULTS ACCORDING TO TYPE OPERATION

No		OPERATED	LOST	DEATH					GOOD	SATIS	POOR	
				IMMED	1 Yr		FOLLOWED	EXCELL				
					Discharged Ulcer	Dead		Discharged Ulcer				Dead
7 Yrs Followed												
1940	III	40	3		1	30	7	21	7	1		
	IV	8	1	1	1	8	1	1		3		
	Total	48	4	1		41	8	22	7	4		
1941	III	24			1	3	3	18				
	IV	2				1			1			
	IVA	13	1		1	14		11	1			
	Total	39	1			18	3	29	2			
6 Yrs Followed												
	III	74	5	5	2	61	12	38	9	1		
	IV	9	1	1	1	6	1	1	1	3		
	IVA	16	1		1	14	2	11	1			
	Total	99	7	7	4	81	15	50	11	4		
1942	III	49	1	2		46	8	44	8	2		
	IV											
	IVA	12				1	1	2	5	1		
	Total	61	1	2		47	9	46	13	3		
5 Yrs Followed												
	III	123	6	8		107	17	73	14	3		
	IV	9	1	1	1	6	1	1	1	3		
	IVA	25	1		1	24	7	16	6	1		
	Total	157	8	9	2	137	25	90	21	7		
1943	III	47	1	1	1	44	9	29	6	1		
	IV											
	IVA	8	1			5		3				
	Total	55	2	1	1	49	11	32	6	1		
4 Yrs Followed												
	III	170	7	9	3	151	26	101	20	4		
	IV	9	1	1	1	6	1	1	1	3		
	IVA	4	2		1	21	5	19	6	1		
	Total	213	10	10	5	178	32	121	27	8		
1944	III	47		2	2	41	13	18	7	1		
	IV											
	IVA	13				12	4	7				
	Total	60	0	2	2	53	17	25	7	1		

regular work. The exceptional case was an individual who gave a poor work record for many years, and also was suffering from pyro boneurism.

There were eight patients, 3.4 per cent, classified as poor in Series I who had Group III operation. Two patients, 86 per cent, were found to have recurrences. Two, 86 per cent, gave a history of postoperative hemorrhage. Four patients stated they were in poor health and had symptoms that did not permit their classification in the excellent, good, or satisfactory groups.

The following is a brief summary of the eight patients who had Group III operation in Series I and were classified as unsatisfactory.

CASE 1 (No. 747743).—L. B., male, aged 49 years, with diagnosis of active duodenal and gastrojejunal ulcer. The patient had typical ulcer history of twenty-seven years duration. Gastrojejunostomy had been performed in 1937. He was admitted May

TABLE VI—Continued

YEAR	OPERATED	LOST	DEATH		IF FOLLOWED BY KILL.	BOND	TIN	TINOR	
			5 Y	Followed					
III	17	7	1	6	10	41	119	97	3
IV	9	1	1	1		1	1	1	3
IVA	47			1	44	0	4	9	
Total	73	10	14	8	54	51	126	20	6
1945 III	40		1		39	7	—	7	3
Jan IV									
July IVA	13	1		1	11	3	1		
Total	53	1	1	1	50	10	—		3
			5 Y	Followed					
III	3	7	12		41	45	141	34	9
IV		1	1	1		1	1	1	3
IVA	60	3			53	14	50	10	1
Total	25	11	14	9	44	1	17	43	13

From II Gastric and Peptic

NOTE: 11 CARRIES AND FOLLOWS									
1940 III	13	1	1	5	10		7		1
III	13	1	1	5	10		7		1
1941 III	14		1	1	10	1	9	1	
III	99	7	6	5	Followed	4	40	1	1
1942 III	15	1	1	1	1			3	
III	44	4	5	5	5 Year Followed	3	22		1
1943 III	16	0			14	1	7	5	1
III	60	4	3	7	46	4	99	11	
1944 III	1	0		1	1	4	11	3	0
III	81	4	3	5 Year Followed	1	8	40	14	
1945 III	9	0	0	1	8	1	6	1	0
Jan									
Jul									
Total	50	4	5	9	72		46	13	

In 1944 with history of hematemesis, melena, and epigastric pain. Hemorrhage occurred on five occasions prior to admission during the previous year. He was operated upon on May 15, 1944, at which time 75 per cent gastric resection, as done. The weight of the resected specimen was 135 Gm. Operative findings: one gastroduodenal ulcer perforated onto colon and active duodenal ulcer.

The patient was readmitted on Oct. 5, 1944, because of epigastric pain and hematemesis. Transfusion was given and he was treated conservatively.

The third admission was for acute onset of paroxysmal atricular fibrillation and hypertension. At this time the ulcer symptoms were well controlled by medical management. The patient's fourth admission on March 22, 1945, was for recurrence of epigastric pain and melena. He again treated conservatively.

He was readmitted for the fifth time because of persistence of epigastric pain and recurrent hematemesis. X-ray examination showed presence of duodenal ulcer. The patient

as re-operated pos Ma 1 1943, at which time gastrojejunal ulcer was found, and 17 Gm of stomach is removed.

The patient last seen the outpatient department in May 1947 at which time he was feeling well.

CASE 2 (No. 633361)—R. D. male, aged 37 years, with diagnosis of obstructed duodenal ulcer. The patient had typical ulcer history for fifteen years. He was admitted to the hospital May 7 1941, with history of recurrent attacks of vomiting and severe epigastric pain. X-ray examination showed duodenal ulcer with fairly high grade obstruction. He had free acid 81 degrees. He was operated pos on May 13, 1942. Weight of the removed specimen 220 Gm. Operative findings were large stomach with indurated pylorus and posterior wall duodenal ulcer perforated into pancreas with considerable inflammatory reaction around entire duodenum.

The patient did quit ill until December 1947 when he had recurrence of epigastric pain and lost weight. Physical examination was negative, except for blood pressure of 110/135. X-ray examination revealed what is believed to be carcinoma of the residual gastric pouch. Because of these findings he was re-operated upon on May 15, 1947. A stomach ulcer found with considerable inflammatory reaction around the anastomosis. The proximal jejunal loop somewhat longer than usual. An additional amount of stomach removed and short loop stomach made.

CASE 3 (No. 633361)—E. H. male, aged 24 years, was admitted to the hospital Sept. 29 1940, with diagnosis of chronic duodenal ulcer. He had typical ulcer history of ten years duration. Marginal ulcer of perforated duodenal ulcer had been done three years prior to admission. The patient had free acid 90 degrees. He was operated upon on Sept. 30, 1940. Weight of the removed specimen was 157 Gm. Operative findings were posterior wall duodenal ulcer perforated into pancreas and an anterior wall ulcer in just position of pylorus. This necessitated closure of an open duodenum. The patient made uneventful recovery.

The patient as schizophrenic on repeated examinations postoperatively. Three years after operation he began to have constant growing epigastric pain, and at the same time had hematemesis and fatty stools. In answer to the questionnaire the patient stated he continued to have epigastric pain, observed restricted diet eats small meals frequently and has occasional vomiting. He was admitted Oct. 9 1947 with small bowel obstruction and was operated upon. No marginal ulcer found at operation. X-ray examination was negative. He has felt relief since.

CASE 4 (No. 667661)—W. G. male, aged 41 years, was admitted Feb. 13, 1943, with diagnosis of chronic duodenal ulcer with obstruction. He had typical ulcer history of fifteen years duration. He had three episodes of hematemesis and melena in the year prior to admission, no epigastric pain and constant vomiting occurred prior to admission. X-ray examination revealed presence of a 1 1/2 inch duodenal ulcer with some obstruction. He had free acid 40 degrees. The patient was operated upon on Feb. 23, 1943. Weight of the removed specimen was 10 Gm. Operative findings were supraduodenal ulcer with marked scarring.

He did very well postoperatively, returned to his farm work, and had no digestive distress. Postoperative anal dilatation was later showed free acid to 80 degrees.

On March 4 1947 he began to have fatty stools and noted onset of edema. When he reported to the clinic one week later on examination and gastroscopy did not reveal presence of ulcer. He was treated conservatively.

On the last visit clinic July 13, 1947 he was asymptomatic and has remained all since this episode of hematemesis.

CASE 5 (No. 781201)—J. W. male, aged 42 years, was admitted March 21, 1947 with a diagnosis of duodenal ulcer with obstruction. He had typical ulcer symptoms for ten years, consisting of epigastric pain, nausea, vomiting, hematemesis and melena were

present on two occasions. She was operated upon on April 4, 1943. Weight of the resected specimen was 223 Gm. Operative findings were posterior wall duodenal ulcer perforated into pancreas. The closure of the duodenum was difficult. Postoperative course unremarkable. The closure of the duodenum was difficult. Postoperative course unremarkable. The closure of the duodenum was difficult. Postoperative course unremarkable.

The patient was readmitted to the hospital on Oct. 4, 1943, at which time she had evidence of small bowel obstruction. At operation of duodenum and jejunum of small bowel were found. This accumulated resection of four feet of small bowel.

She was last seen February 1947 when she complained of pain after meals and vomiting. She observed dietary restriction and was unable to frequent small feedings. Her height was 5 feet 3 inches and she weighs 101 pounds. She appears considerably underweight. X-ray examination shows dilatation of gastrojejunal anastomosis. No evidence of recurrent ulceration.

This patient has many home difficulties and is stressed nervously. Her mother has limited her to some degree. It may be that in the event her emotional problems were alleviated, the general health would improve.

CASE 6 (X 4044)—R. M. man, aged 42 years, was admitted March 14, 1941. There was typical ulcer history of three years duration. He complained of dull constant epigastric pain and weight loss. The preoperative acid was as high as 45 degrees. The patient was operated upon March 1941. The weight of the resected specimen was 153 Gm. Operative findings were posterior wall duodenal ulcer perforated into pancreas.

Postoperative the patient was unable to gain weight and had multiple complaints such as epigastric pain, poor appetite and marked weakness. X-ray examinations have been negative for presence of recurrent ulcer.

In 1944, the patient was hospitalized on the neurology service because of pain in the back and legs. Pathology of both arms and legs was found and decreased hearing in left ear. Diagnosis of primary lateral sclerosis was made.

On May 1, 1947, local doctor reported X-ray examination at this time showed no evidence of ulcer.

CASE 7 (X 757641)—A. M. man, aged 42 years was admitted Nov. 27, 1942, with diagnosis of duodenal ulcer. He had typical ulcer history of thirteen years duration. He complained of epigastric pain and occasional vomiting. The preoperative acid was as high as 51 degrees. He was operated upon Dec. 1, 1942. Weight of the resected specimen was 263 Gm. Operative findings were anterior wall duodenal ulcer.

The patient did not report for periodic checkups. This might be due to the fact that he resided in Yelm, Wash. In answer to the questionnaire, he stated that his health was poor and he had frequent diarrhea and bloating distress. He was unable to carry on his work. Repeated requests for him to return for follow up and examination have not been answered.

CASE 8 (X 718147)—A. T. man, aged 37 years, was admitted May 3, 1944, with diagnosis of duodenal ulcer with obstruction. He had typical ulcer history of nine years duration. He complained of epigastric distress, vomiting and anorexia. Fasting specimen showed 33 degrees of free acid. He was operated upon May 5, 1944. The resected specimen weighed 220 Gm. Operative findings were posterior wall duodenal ulcer.

The patient had been operated upon in 1940, and is suffering from postoperative effect.

He last reported to the surgery June 5, 1944, at which time he complained of abdominal distress and diarrhea. It is necessary for him to limit the size of meals and eat frequently. He also complained of feeling weak and tired. X-ray examination showed no evidence of recurrence.

It is felt that because the patient had had meningitis it might be a contributing factor as to the state of health at this time. The patient was considered as unsatisfactory result on the basis of the complaint.

In the two patients who developed recurrent ulcers it was felt that criteria for a satisfactory operation had not been met. One patient (I B Case 1) had an inadequate resection done. Because 6 cm of jejunum were included in the 12.5 Gm. weight of the resected specimen, the actual weight was 135 Gm. This amount is far below the average weight of resected specimens. The other case (I D Case ) developed recurrent ulcer because the proximal loop was longer than usual.

#### RESULTS IN THE GROUP IVA OPERATION IN SERIES I DUODENAL ULCER CONTROL JEJUNAL ULCER

There were 65 patients with Group IVA operation followed in Series I. Eighty per cent of these patients were enjoying very good health. Ten patients, 18 per cent of the cases were classified satisfactory. One patient, 1.8 per cent of the cases followed was classified a poor result because of a recurrent gastric jejunal ulceration.

Following is a case summary of the one patient who had Group IVA operation in Series I and was classified poor.

W. P. (X 64790) male aged 55 years had six hospital admissions. The first admission was on Sept. 4 1940 at which time he gave a history of peptic ulcer of forty four years duration. Symptoms began at 14 years of age. He had had six severe hemorrhages prior to admission to the hospital on Sept. 24 1940. In 1920, the patient had had gastric jejunostomy performed. Subsequent to this he had three severe episodes of bleeding.

On Sept. 4 the patient was hospitalized because of presence of anemia, tarry stools, and drop in hemoglobin. In known bleeding peptic ulcer. He was treated conservatively with good results.

The second admission was on Aug. 6, 1941. At that time he was readmitted for consideration of surgical treatment for chronic duodenal ulcer and possible anemia. He had continued to have gastric hemorrhages since the last admission. He had had little or no interest in the food. The patient had been very cooperative, followed the diet well, had taken very good care of himself. In view of the recurrent hemorrhages, gastrectomy was the treatment of choice. He was operated upon on Aug. 11, 1942. The operative findings were as follows: There was considerable induration in the neighborhood of the duodenum. Quiescent gastrojejunal ulcer was present. Because of the large amount of induration surrounding the duodenum, it was felt that in this case Group IVA operation should be done. The weight of the resected stomach was only 75 Gm. However, although the stomach was very small, the record suggests that only a 60 per cent resection was accomplished.

The third admission was for treatment of Colles' fracture involving the right wrist.

The patient was admitted for the fourth time on Oct. 1 1943. At that time he complained of the recurrence of tarry stools beginning on Sept. 30 1943. This was preceded by three weeks of mild abdominal distress. It was believed the patient had bleeding stomach ulcer. He was treated conservatively with continuous intragastric drip of milk and cream and 10 cc of Trisodium. On conversion therapy the patient's bleeding stopped and he was discharged on Oct. 29 1943.

He was readmitted for the fifth time on April 22, 1944. He had been doing quite well on medical regimen, but was admitted this time for treatment of nocturnal orthostatic dyspnea. Diagnosis at this time was primary hypertension and quiescent gastrojejunal ulcer.

The sixth admission was on Nov. 11 1946. At that time the patient complained of epigastric pain coming on late after meals and relieved by food and alkaline medication. On Nov. 13, 1946, the patient was operated upon and bilateral esophagogastric anastomosis

as done. X-ray examination on J ~~une~~, 1941 showed absence of any evidence of pathology except for rather slow emptying into the jejunum. Patient is apparently not having any difficulty and has resumed his occupation.

It has been stated by Lewisohn<sup>22</sup> that in order to achieve satisfactory results the duodenal ulcer must be removed. However in the cases followed and studied here with Group IV A operation where the ulcer was left in situ the results were gratifying in that a low percentage of poor results was found. In the one poor case 18 per cent of the patients in Series I with Group IV A operation, it was found that the patient developed a recurrence because an inadequate resection was done.

The question may naturally be asked as to why recurrent ulcers are a problem if the criteria for a satisfactory operation for ulcer have been followed. One may answer this by self-inquiry. Have the criteria been followed? Thus, a surgeon after a long tedious battle with the intra-abdominal contents of a short fat hypersthenic individual, may in his own mind feel that he has done a good operation. However it is in that type of individual where the stomach is small and transverse in nature and tethered along the diaphragm making exposure difficult that one cannot *feel* but instead should be mathematically certain that an adequate amount of stomach has been taken. It is our practice in the Clinic to excise at least 175 Gm. of stomach. This point was not followed in two cases (L. B. N. 4345 and W. P. No. 609799). Both of these patients fell into the category just mentioned. Naturally one would surmise that if recurrences are to be had, they will occur in individuals where in the criteria have not been met. It is our belief that this was the cause of recurrent ulcer in these two patients—that is, not excising enough stomach.

#### RESULTS OF GROUP IV OPERATIONS

Since this study is an evaluation of 416 patients consecutively operated upon from Jan. 1, 1940 the results of the Group IV operation were also included. It was quickly appreciated that this procedure was unsatisfactory in the treatment of duodenal ulcer and therefore it was discontinued early in 1941.

Follow-up studies were carried out on six patients. There were two additional patients operated upon in 1940 who had Group IV operation and then were re-operated upon within a six month period. They have been included in the patients followed that had Group III operation.

Of the six patients on whom follow-up was done three were doing well. The remaining three were found to be poor.

The following is a brief summary of the three cases in which Group IV operation was done.

CASE 1 (X 804072) —O. J. ~~man~~, aged 24 years, was admitted April 6, 1940, with diagnosis of duodenal ulcer. He had typical ulcer history of two years duration and complained of severe epigastric pain. The patient was operated upon April 11, 1940. The specimen measured 14 sq. cm. Operative findings were anterior wall duodenal ulcer with good deal of surrounding induration.

Postoperatively the patient did well and was inducted in the Army on March 1, 1941. He received medical discharge on Oct. 22, 1942, because of marginal ulcer. Surgery was done by the Veterans Administration and marginal ulcer found.

CASE 2 (No. 601443)—O M woman, aged 46 years, as admitted with typical history of duodenal ulcer on May 4 1940. She previously had surgical repair of perforated ulcer 1920 and gastroyejunosotomy in 1926. The patient continued to have intermittent period of epigastric pain. In February 1940, she had severe hemorrhage and onset of severe epigastric pain. She was operated upon May 24, 1940, with Group IV operation. Operative findings were anterior and posterior wall duodenal ulcer. Weight of the resected specimen was not given. (Specimen greater curvature 13 cm. lesser 7 cm. proximal loop of resection 45, distal 65.)

The patient did fairly well but had episodes of acute epigastric pain associated with ingestion of food and fatty foods. On Sept. 28, 1941, cholecystectomy was done. Diagnosis as chronic cholecystitis and calculi etc. She felt fairly well subsequently until February 1946, when she began to have severe epigastric pain, melena, and extreme exhaustion. In the summer of 1946 she had melena and repetition of this in November 1946.

She was readmitted on Jan. 3, 1946 and reoperated upon Jan. 13, 1947 with Group III operation. Operative findings are long proximal loop 45 cm. plus 10 cm. of enterostomum. Distance from proximal side enterostomum was 16 cm. total length 10 cm. from ligament of Treitz to gastroyejunal anastomosis. Diagnosis was gastroyejunal ulcer.

CASE 3 (No. 666070)—H L man, aged 53 years was admitted April 23, 1940 with typical history of duodenal ulcer of thirty years duration. The symptoms are epigastric pain, bloating, and weight loss. He was operated upon April 7 1940. Operative findings were anterior wall duodenal ulcer with considerable induration. Weight of the resected specimen as not given.

and then began to have epigastric pain, and the pain in July 1947 complaining July 19 1947 and reoperated upon July 23, at which time the atrial segment was excised. The patient previously had had long proximal loop and an enterostomum. Thus as excised the segment of stomach and short proximal loop was made.

#### RESULTS OF EXPLANTATION OF THE TYPE OF OPERATION HISTORIC AND PYLORIC VICINE

Because handling of the duodenum presents no technical problem, all the patients in this series were treated by Group III operation.

Of the 72 cases in which follow up study was done 63, or 8 per cent, of the patients were feeling very well 13 or 1 per cent were classified satisfactory and 7 per cent were poor.

No recurrences were found in this series.

The following is a brief summary of the two cases in this series which were classified as unsatisfactory.

CASE 1 (No. 723751)—H B man, aged 54 years, was admitted to the hospital June 19 1943. He had typical history for eight years. Symptoms consisted of epigastric pain, nausea, and vomiting. The patient had been performing gastric lavage for period of eight weeks. He was admitted in view of symptoms with extraintestinal results. The patient was very malnourished. He was operated upon June 14, 1943, after the alkalosis had been corrected and blood urea nitrogen had returned to normal. The resected specimen weighed 360 gm. Operative findings are peptic ulcer and an extraintestinal extraintestinal obstruction of stomach and duodenum.

Postoperatively there was some improvement but the patient has never been free of pain. He has occasional nausea and vomiting, must eat frequent small meals, and vomit sour foods. He is also subject to periods of mental depression and has arthritis of severe degree.

CASE (N 70451)—E. L. male, aged 47 years was admitted to the hospital on Dec 8 1940, with five week history of acute onset of epigastric pain, anorexia, nausea. The preoperative diagnosis was probable carcinoma of the stomach. The patient was operated upon on Dec 16, 1940. Weight of the resected specimen 300 gm. Operative findings were benign gastric ulcer of the mid portion of the lesser curvature base of the ulcer was  $\frac{1}{2}$  by  $1\frac{1}{2}$  cm.

Postoperatively the patient did fairly well for four weeks. In June 1943 he began to have more difficulty. Underweight complained of distress after meals and nausea. observed many dietary restrictions, and ate frequent small meals. The patient has been requested to return to the clinic by letter and even telephone in July 1943 but he fears further surgery and is reluctant to return.

# OBSTRUCTED AND NONOBSTRUCTED CASES

Sanders, in reviewing his cases noted that the result in patients who had been obstructed prior to gastrectomy were better than in nonobstructed patients. We were interested in determining if this observation was true in our cases. Table VII indicates results in obstructed and nonobstructed patients in Series I and II.

TABLE VII RESULTS OF OBSTRUCTED AND NONOBSTRUCTED CASES

	RESULTS				EXCELLENT		GOOD		FAIR		POOR	
	OPERATED	LOST	IMMEDIATE	LATE	POORLY	EXCELLENT	GOOD	FAIR	POOR	POOR	POOR	POOR
		6 mo	1 yr	admission	1 yr	1 yr	1 yr	1 yr	1 yr	1 yr	1 yr	1 yr
Obstructed	44	1	4		1	34	1	1	1	1	1	1
Nonobstructed	44	1	10		14	34	1	1	1	1	1	1
Total cases	88	2	14		15	68	2	2	2	2	2	2

Series II Gastric and Duodenal Ulcer												
Obstructed	11		1	1		1	3	1	1	1	1	1
Nonobstructed	9	4	3		64		41	14	1	1	1	1
Total cases	20	4	4				44	15	2	2	2	2

No appreciable difference was noted in result between obstructed and nonobstructed patient except for a slightly higher percentage of poor cases among the obstructed patient. (See Table VII A.)

TABLE VII A

RESULTS	OBSTRUCTED		NONOBSTRUCTED	
	NUMBER	PERCENT	NUMBER	PERCENT
Excellent	6	11	1	13.1
Good	14	3	37	60.0
Satisfactory	47	16.5	17	13.8
Poor	9	11	3	6.1
Total	76	100	58	100

# POSTOPERATIVE HEMOGLOBIN VALUES

Table VIII indicates 347 postoperative hemoglobin determinations for patients according to sex. It also shows the results of the number of years follow-up study was carried out.



CASE 2 (N 601447)—O M woman, aged 48 years, as admitted with typical history of duodenal ulcer on May 4, 1940. She previously had surgical repair of a perforated ulcer in 1920 and gastrectomy in 1926. The patient continued to have intermittent periods of epigastric pain. In February 1940 she had severe hemorrhage and onset of severe epigastric pain. She was operated upon May 4, 1940 with Group IV operation. Operative findings were a tense and posterior all duodenal ulcer. Weight of the resected specimen was not given. (Specimen greater curvature 19 cm. lesser 7 cm. proximal loop of resection 4.5, distal 6.5.)

The patient did fairly well but had episodes of severe epigastric pain associated with ingestion of fried and fatty foods. On Sept. 25, 1941, hysterectomy was done. During months of chronic cholecystitis and cholelithiasis she felt fairly well subsequently until February 1946, when she began to have severe epigastric pain, indigestion, and extreme bloating. Again in the summer of 1946 she had melena and repetition of this in November 1946.

She was readmitted on Jan. 1, 1947 and reoperated upon Jan. 13, 1947 with Group III operation. Operative findings were long proximal loop 45 cm. plus 10 cm. of entero-anastomosis. Distance from proximal side enteroanastomosis was 15 cm. total length 70 cm. from ligament of Treitz to gastropyloric anastomosis. Duodenum was gastropyloric ulcer.

CASE 3 (N 605420)—H L, a man, aged 63 years, admitted April 23, 1940, with typical history of duodenal ulcer of thirty years duration. The symptoms were epigastric pain, bloating, and weight loss. He was operated upon April 27, 1940. Operative findings were anterior. II duodenal ulcer with considerable induration. Weight of the resected specimen was not given.

The patient did fairly well but no far and then began to have epigastric pain, bloating, and had to restrict his diet. He returned to the clinic in July 1947 complaining of the symptoms mentioned. He was readmitted July 19, 1947 and reoperated upon July 24, at which time the antral segment was removed. The patient previously had had long proximal loop and an entero-anastomosis. This was revised with segment of stomach and short proximal loop was made.

#### RESULTS OF SERIES B—COMING TO TYPE OF OPERATION GASTRO AND PYLORIC ULCER

Because handling of the duodenum presents no technical problems, all the patients in this series were treated by Group III operation.

Of the 70 cases in which follow-up study was done 55 or 76 per cent, of the patients were feeling very well, 15 or 1 per cent were classified satisfactory and 10, or 7 per cent were poor.

No recurrences were found in this series.

The following is a brief summary of the twelve cases in this series which were classified as unsatisfactory:

CASE 1 (N 713781)—H B, man, aged 55 years, as admitted to the hospital June 18, 1943. He had typical ulcer history for eight years from onset consisted of epigastric pain, nausea, and vomiting. The patient had been performing gastric lavage for period of eight weeks. He was admitted in state of shock with extramural antrum. The patient was very malnourished. He was operated upon June 18, 1943, after the alkalies had been corrected and blood urea nitrogen had returned to normal. The resected specimen weighed 300 Gm. Operative findings were pyloric ulcer and an extramural extramural obstruction of stomach and duodenum.

Postoperatively there was some improvement but the patient has never been too well. He has occasional nausea and vomiting, must eat frequent small meals, and avoids fatty foods. He is also subject to periods of mental depression and has rickets of severe degree.

## POSTOPERATIVE DIGESTIVE DIFFICULTIES

Table XIV shows the number of patients that had any digestive difficulty as reported by years for Series I and II respectively

**Multiple complaints** refers to those patients who had more than one digestive complaint. None refers to the patient who had no complaints, except for single minor complaints as listed.

There were 364 patients followed in Series I and II. Of these, 311, or 86 per cent of the patients had no digestive difficulty whatsoever. Minor symptoms were found in 37 or 10 per cent of the cases. Sixteen patients, or 4 per cent of the cases, had multiple complaints.

Follow-up was done on 290 patients in Series I. Of these 83.6 per cent were asymptomatic. Minor complaints were found in 10.3 per cent of the cases, and 4.1 per cent of the patient had multiple complaints.

Seventy-two patients were followed in Series II. 84.7 per cent were without digestive difficulties. 9 per cent had minor complaints and 5 per cent had multiple complaints.

## DUMPING SYNDROME

The success or failure of operative procedures for ulcer in the past has been evaluated mainly on the basis of recurrent ulceration. This is the most important consideration. However in recent years, a considerable awareness has occurred that there are patients who may suffer from symptoms which may to a greater or lesser degree deprive the patient of a good result even in the absence of recurrent ulceration.

Realization that some disturbing symptom followed anatomic alterations in the normal stomach and small bowel relations was noted by Hertz<sup>14</sup> in 1913. He observed the symptom of sensation of fullness in a patient with a gastrojejunostomy. The symptoms were severe enough to force the patient to decrease the intake. He also noted in this patient, on fluoroscopic examination that the stomach emptied rapidly and that there was an associated distention of the jejunum. Hertz believed that the distress was occasioned by this rapid emptying and sudden distention. He stated that the patient obtained relief by lying down and believed that the reason for this was the fact that with the patient prone the stomal opening was no longer the most dependent portion of the stomach.

Mix<sup>15</sup> stated that in patient in whom distress arose of the nature just described following gastrojejunostomy the symptoms were relieved by taking down the gastrojejunostomy and restoring normal gastrointestinal continuity.

With the increase in the number of subtotal gastric resections being done for peptic ulcer these postprandial symptoms have been the subject of much discussion.

Eusterman and Balfour<sup>16</sup> stated that the symptoms were due to too rapid emptying.

Spell<sup>17</sup> mentioned the syndrome but believed it disappeared after the jejunum became accustomed to the new anatomic arrangement. Glaeser<sup>18</sup> stated that the symptoms were on the basis of hyperglycemia in some of the patients within the first half hour following the meal.

TABLE XIII POSTOPERATIVE HEMOGLOBIN VALUES

	2 YEAR		3 YEAR		4 YEAR		5 YEAR		6 YEAR		7 YEAR	
	MALE	FEMALE	MALE	FEMALE	M	F	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
Normal	3	3	4	3	1	1	3	3	1	6	6	6
Underline	1	3	4	5	1	1	3	3	9	3	0	1
Normal	70	14	41	11	34	6	49	6	19	1	24	1
Total	NJ	20	49	19	40	8	54	11	29	4	34	8
Total cases	103		63		48		63		34		40	

Normal, hemoglobins greater than 13.5 Gm. values as high as 17 Gm.

Underline, hemoglobins are less than 11 Gm. but less than 12.5 Gm.

Anemia, hemoglobins less than 11 Gm.

It was found that two years following surgery the males showed a normal hemoglobin in 93.6 per cent of the cases as compared to 70 per cent in the females. At three years, 83.4 per cent males had normal hemoglobins, whereas the females totaled 57.8 per cent. Normal hemoglobins were found in the males in 95 per cent of the cases as contrasted with 7 per cent in the females at four years. At five years, the males had normal hemoglobin in 90.7 per cent of the cases as compared to 54.5 per cent in the females. Ninety five per cent of the males and only .3 per cent of the females had normal hemoglobins at six years. Seven years following surgery hemoglobins were found to be normal in 100 per cent of the males, and 83 per cent of the females.

There was a marked difference in hemoglobin values between males and females as shown through the entire seven-year follow-up. Males appeared more capable of maintaining normal hemoglobins.

In the patients who were not bleeding from a recurrent ulcer only one case was encountered of severe anemia which did not respond to iron therapy. This was the case of a woman who had a hemoglobin value of 6½ Gm. The cause of anemia could not be determined because of the patient's refusal to have further studies done.

#### POSTOPERATIVE WEIGHT CHANGES

There was a significant number of patients who had difficulty maintaining what would be considered normal weight. Although the inability to gain weight in patients who have had subtotal gastric resections is not uncommon, symptoms arising from this are rare.

Table XIII A indicates the weight changes that occurred in Series I and II.

TABLE XIII A POSTOPERATIVE WEIGHT CHANGES

SERIES	NUMBER WHO LOST WT.	WT.		NO CHANGE
		GAINED (POUNDS)	LOST (POUNDS)	
I	134	14	106	34
II	47	14	17	3
Total	201 (87%)	13.6	123 (23.6%)	37 (7.3%)

has had the occurrence of neither the occurrence of  
ulcers (N. H. N. 84718) operated upon in 1931  
had gastrectomy done in 1947, followed by

Lapp and Dibold<sup>16</sup> in 1933 called attention to the presence of hypoglycemia two and one-half hours following a meal. They found that in performing glucose tolerance tests on gastrectomized patients, there was an abnormally high rise above normal in blood sugar values within the first hour followed by a hypoglycemia two to two and one-half hours later.

Schwartz, Rheingold, and Veeh<sup>17</sup> were unable to correlate the level of blood sugar with the appearance of symptoms, and they believed symptoms to be based on distention of the upper part of the small bowel. Custer Butt and Waugh also favored this as being the important factor.

A definite pattern of symptoms has been noted in the gastrectomized patient. These symptoms occur during the progress of eating immediately after or within one-half hour after finishing the meal. The patient becomes distended and has a sensation of fullness in the epigastric region. A feeling of an unpleasant sensation of general warmth occurs, and with this the occurrence of cold sweat mainly on the forehead. Some of the patient complain of weakness or fatigue; others feel very sleepy. There is an associated cardiac palpitation and the patient may appear very pale. To the previously described symptoms has been given the name dumping syndrome. The name has been derived from the fact that it was believed the rapid dumping of food into the jejunum and resulting distention was responsible for this effect.

The incidence of dumping syndrome has variously been reported as varying from 5.6 to 7 per cent. Jordan<sup>18</sup> reported that dumping syndrome and recurrent ulcer accounted for 5 per cent of the unsatisfactory results following partial gastrectomy.

Miller<sup>19</sup> noted an incidence of 1 per cent in his cases. Custer and associates<sup>20</sup> reported .8 in 500 cases, or .6 per cent. Mateer<sup>21</sup> commenting on Jordan's paper stated an incidence of 14 per cent.

Custer Butt and Waugh felt that the size of the stomach was related to the symptoms and modified the operative procedure from a Polya in which the entire cut end of the stomach is used for the anastomosis. He changed this to a Hofmeister modification in which the lesser curvature is inverted, reducing the size of the stomach. He subsequently noted that when dumping syndrome appeared it was less severe and disappeared within a short time. Table XV shows the cases of dumping syndrome in Series I and II. Eleven patients, or 6 per cent complained of symptoms of dumping syndrome. In no case were the symptoms of a severe degree but rather could be classified as moderate or mild in nature. With the exception of one patient (I-8) all the patients were able to maintain normal nutrition. These patients had to make some adjustment in their dietary intake and usual routing. They found that decreasing the size of the meals, avoiding liquid with meals, and eating more frequently diminished their symptoms. Others learned that resting immediately after eating would tide them over the period of discomfort.

#### POSTOPERATIVE QUANTITY OF FOOD INTAKE

Table XVI shows the number of patients followed for each year and the ability to observe normal eating habits with regard to quantity and regularity for Series I and II respectively.

TABLE XIV POSTOPERATIVE DIAGNOSIS IN RUPTURE

YEAR	AGE	SEX	REFUSED	O	POL. LOWERED	MULTIPLE		X I W A	BLOAT	HIFART	MATERIAL	PAIRS	DOWNS
						ALL	CONC						
Series I Intra-abdominal Ulcer													
1940	48	J	4	4	41								
1941	51	B	3	3	44				1	1			
1942	61	B	1	1	58				3				
1943	87	B	2	2	19				1	1			4
1944	60	B			54				1	1			
1945	83	B	2	1	80				1	1			
Total	136	23	11	11	202			4	4	1	1	2	1
Series II Gastric and Duodenal Ulcers													
1941	33	B	1	1									
1942	34	B			10								
1943	15	B	1	1	13								
1944	16	B			14								2
1945	21	B	1		18								
1946	8	B	1		8								
Total	80	14	4	4	53								
Series III Gastric and Duodenal Ulcers													
1941	33	B	1	1									
1942	34	B			10								
1943	15	B	1	1	13								
1944	16	B			14								
1945	21	B	1		18								
1946	8	B	1		8								
Total	80	14	4	4	53								

\*Of these, 21 per cent (334 patients) had multiple ulcerations, 18 per cent (272 patients) had multiple ulcerations, and 18 per cent (272 patients) had multiple ulcerations.

per cent (272 patients) had multiple ulcerations, and 18 per cent (272 patients) had multiple ulcerations.

Lapp and Dibold<sup>19</sup> in 1933 called attention to the presence of hypoglycemia two and one-half hours following a meal. They found that in performing glucose tolerance test on gastrectomized patients, there was an abnormally high rise above normal in blood sugar values within the first hour followed by a hypoglycemia two to two and one-half hours later.

Schwartz, Rheingold, and Neebeles<sup>20</sup> were unable to correlate the level of blood sugar with the appearance of symptoms, and they believed symptoms to be based on distention of the upper part of the small bowel. Custer Butt and Waugh<sup>21</sup> also favored this as being the important factor.

A definite pattern of symptom has been noted in the gastrectomized patient. These symptoms occur during the progress of eating immediately after or within one-half hour after finishing the meal. The patient becomes distended and has a sensation of fullness in the epigastric region. A feeling of an unpleasant sensation of general warmth occurs, and with this the occurrence of cold sweat mainly in the forehead. Some of the patient complain of weakness or fatigue others feel veryleep. There is an associated cardiac palpitation, and the patient may appear very pale. To the previously described symptoms has been given the name dumping syndrome. The name has been derived from the fact that it was believed the rapid dumping of food into the jejunum and resulting distention was responsible for this effect.

The incidence of dumping syndrome has variously been reported as varying from 5.6 to 7 per cent. Jordan<sup>22</sup> reported that dumping syndrome and recurrent ulcers accounted for 1.2 per cent of the unsatisfactory result following partial gastrectomy.

Miller<sup>23</sup> noted an incidence of 7 per cent in his cases. Custer and associates<sup>21</sup> reported 2.3 in 500 cases, or .6 per cent. Mateer<sup>24</sup> commenting on Jordan's paper stated an incidence of 14 per cent.

Custer Butt and Waugh<sup>21</sup> felt that the size of the stoma was related to the symptoms and modified the peroral procedure from a Polya in which the entire end of the stomach is used for the anastomosis. He changed this to a Hofmeister modification in which the lesser curvature side is inverted reducing the size of the stoma. He subsequently noted that when dumping syndrome appeared it was less severe and disappeared within a short time. Table XV shows the cases of dumping syndrome in Series I and II. Eleven patients, or 2.6 per cent complained of symptoms of dumping syndrome. In no case were the symptoms of a severe degree but rather could be classified as moderate or mild in nature. With the exception of one patient (I-8) all the patients were able to maintain normal nutrition. These patients have had to make some adjustment in their dietary intake and usual routing. They found that decreasing the size of the meals, avoiding liquid with meals, and eating more frequently diminished the symptom. Others learned that resting immediately after eating would tide them over the period of discomfort.

#### POSTOPERATIVE QUALITATIVE FOOD INTAKE

Table XVI shows the number of patients followed for each year and their ability to observe normal eating habits with regard to quantity and regularity for Series I and II respectively.

The term three regular meals implies that the patient eats regularly and his intake is the average amount of normal people. The designation three regular meals plan refers to the patient with eat at a regular time whose

TABLE XI. COURSE OF DUCHESS BYEMONE

HOSPITAL NAME, AGE,		OPERATION	WEIGHT OF INFECTED SPLEEN MEN	PREOP WT	POSTOP WT	REMARKS
						and relaxed out 1 hr after meals, mainly after heavy meals
717943 (L.A.) 57 (f)	Duodenal ulcer with obstruct	III 4/1/44	445	104	103	Feels exhausted after meals, rests for ½ hr has slight epigastric distress
726512 (L.K.) 36 (m)	Duodenal ulcer	III 1/19/43	165	146	151	Performs great deal after meals for ½ hr and evening
74 41						
67 43 (f)		12/41				nausea at meals meals relieved by lying down does not occur after every meal
719794 (I.B.) 61 (m)	Duodenal ulcer with hemorrhage & obstruct	III 11/29/44	418	150	115	Following meals has sensation of fullness feels weak and drowsy and must lie down for 15 min
736413 (G.L.) 53 (m)	Unresected stomach ulcer DU	III 11/15/43	265	140	147	Back feeling after meals, weakness, palpitation, and breaths and in cold sweat—lasts ¼ to 1 hr after meals
741443 (T.O.) 53 (m)	Duodenal & gastric ulcer	III 9/20/44	175	150	135	Became sleepy after evening meal, feels somewhat faint and dyspneic, better after lying down for ¼ hr
745617 (A.H.) 56 (m)	Gastric ulcer	III 4/11/43		145	144	No nausea, sickness, flushing of face, palpitation, feels faint, performs freely for 1½ hrs to ¼ hr after meals
Series II						
741447 (C.M.) 50 (m)	Gastric ulcer	III 4/13/44	425	162	150	Weakness and vomiting after meals relieved by lying down, lasts from ¼ to 1 hr
751671 (W.H.) 48 (m)	Gastric ulcer	III 7/17/44	550	145	140	Feels weak and tired after some meals, becoming less severe and less frequent

TABLE XVI POSTOPERATIVE QUANTITATIVE FOOD INTAKE

YEAR	MALES	FEMALES	DEATH	RECORD	FOOD	ED	3 REG. MEALS	3 REG. MEALS +	FRF
				Series I	II	III	IV	V	
1940	45			4	43			1	6
1941	51			3	40			11	
1942	1			1	85			11	5
1943	53				49			15	3
1944	60				54			14	3
1945	39			1	50			1	3
Total	259			11	40			51	21
				Series I	II	III	IV	V	
1940	18			4	10			4	1
1941	14				11			3	
1942	15			1	1				
1943	16				14			2	4
1944	21			3	18			7	
1945	9			1	6			1	
Total	89			14	4			22	5

\*Three regular meals, 19% or 6.8 per cent of total food intake; 3 regular meals plus supplemental feedings, 10 or 3.8 per cent.

†Three regular meals, 45 or 16.5 per cent of total food intake; 3 regular meals plus supplemental feedings, 1 or 3.8 per cent of total food intake; 3 regular meals plus supplemental feedings, 1 or 3.8 per cent of total food intake.

Intake is slightly smaller than normal amounts, and includes supplemental feedings between meals. Frequent small feedings indicates that the patient is unable to take a normal size meal and therefore must eat frequently and smaller amounts.

There was a total of 104 patients followed in Series I and II with regard to quantitative food intake. Of these 44 patients or 6 per cent of the cases, were enjoying three regular meals. 90 patients, or 96 per cent of the cases, ate three regular meals plus supplemental feedings. 3 patients, or 3 per cent were restricted to the amount of food they could eat at one time and also were eating frequently.

There were 29 patients followed in Series II. Of these 69 per cent ate three regular meals. 50 per cent ate three regular meals plus supplemental feedings and 6.8 per cent restricted to frequent small feedings.

In Series II there were 89 cases followed. Of the total, 6.5 per cent of the patients were able to eat three regular meals. 80 per cent ate three regular meals plus supplemental feedings and 6.9 per cent ate frequent small feedings.

#### POSTOPERATIVE FOOD TOLERANCE

Table XVII indicates the number of patients with food intolerances by year for each of the two series.

There were 364 patients followed. The majority of patients followed in the study 60.8 per cent were able to eat all food without restrictions. 34 per cent of the patients were able to eat a regular diet, but had difficulty with single foods. 4.4 per cent observed dietary restrictions for multiple food.

Of the 290 patients followed in Series I 61.9 per cent of the patients ate all foods without any restrictions. 31.5 per cent had no dietary restriction except for single foods. 6.6 per cent observed dietary restrictions for multiple foods.



The term three regular meals implies that the patient eats regularly and his intake is the average amount of normal people. The designation three regular meals plus refers to the patient who eats at a regular time whose

TABLE X. CASES OF DUMPS BY MEAL

HOSPITAL NO NAME, AGE, SEX	DIAGNOSIS	ONSET TRO P	WASHER OF FINGERED SPEC MEN (GM)	PREOP WT (POUNDS)	PRESENT WT (POUNDS)	SYMPTOMS
<i>Series I Duodenal and Ulcer (Gastrojejunal Ulcer)</i>						
717015 (E. L.) 64 (m)	Duodenal ulcer th obstruct	IX 7/2/43	215	128	140	Feels sick and nauseated for about 1 hr after meals, mainly after heavy meals
717965 (L. A.) 57 (f)	Duodenal ulcer with obstruct	III 4/1/44	253	106	102	Feels exhausted after meals, rests for 1/2 hr; has slight epigastric distress
726972 (L. R.) 36 (m)	Duodenal ulcer	III 2/19/43	163	180	195	Perquires great deal after meals for 1/2 hr
736026 (H. H.) 49 (m)	Duodenal ulcer	III 1/23/43	130	145	148	Weakness and vomiting after some meals relieved by lying down
603504 (E. F.) 47 (f)	Duodenal ulcer	III 9/11/43	126	125	114	Weakness, vomiting, nausea for 1/2 hr after meals relieved by lying down; does not occur after every meal
734761 (I. H.) 61 (m)	Duodenal ulcer th hemorrhage & obstruct	III 11/24/44	210	130	115	Following meals has sensation of fullness, feels sick and drowsy and must lie down for 15 min
736435 (G. L.) 1 (m)	(Gastrojejunal stomach ulcer I U)	III 11/18/43	445	195	167	Sick feeling after meals, weakness, palpitation, and breaths out in cold sweat—about 1/2 to 1 hr after meals
741415 (T. C.) 53 (m)	Duodenal & gastric ulcer	III 7/20/44	172	155	155	Becomes sleepy after evening meal, feels somewhat faint and drowsy, better after lying down for 1/2 hr
746557 (A.) 56 (m)	(Gastrojejunal I)	III 4/11/43		195	144	Has anorexia, weakness, flushing of face, palpitation, feels faint, perquires freely for 15 min to 1/2 hr after meals
<i>Series II</i>						
641437 (C. M.) 54 (m)	Gastric ulcer	III 4/11/44	425	145	170	Weakness and vomiting after meals relieved by lying down, lasts from 1/2 to 1 hr
731874 (W. H.) 48 (m)	Gastric ulcer	III 7/17/43	4	140	120	Feels sick and tired after some meals, becoming less severe and less frequent

In Series II of the 72 patients followed, 36 per cent of the patients ate all foods without any restriction. 23.6 per cent had no dietary restriction except for single food and 7 per cent observed dietary restrictions for multiple foods.

It was found that a considerable number of patients were not drinking milk since the operation. The question arose as to whether this was due to an intolerance to milk or merely a dislike because of long usage in medical regimen prior to surgery. Symptoms of intolerance to milk were nausea, feeling of fullness, upper abdominal distress, and vomiting in some cases.

Table XVIII shows patients' tolerance to milk in Series I and II.

Of the 364 patients followed in the two series, 94 patients reported they did not drink milk postoperatively. Twenty-seven patients stated they did not drink milk preoperatively and postoperatively. A definite aversion to milk was noted in 57 patients, or 16.9 per cent. These individuals reported no distress from milk, but had acquired a distaste for it from long usage as a part of the medical regimen. The remaining 37, or 11 per cent, did not drink milk postoperatively because they were intolerant to it.

Eleven patients were studied who stated they were intolerant to milk. A Rafter duodenal tube was passed into the stomach and positioned under fluoroscope so that the end of the tube lay just within the gastric pouch. Then 500 cc. of 37 per cent butt of milk was placed in an ordinary intravenous flask which was completely covered to prevent the patient from knowing what was being administered. This was run in rapidly to simulate the patient's drinking milk under ordinary circumstances.

TABLE XVIII. TOLERANCE TO MILK

YEAR	TOTAL CASES	DEAD	REF. OF MILK	WEL. FED	NO MILK PLEAS- ED	NO OF MILK POSTOP YES	NO OF MILK POSTOP NO	DEF. INTOL- ERANCE
<i>Series I Duodenal Ulcer Gastrojejunal Pile</i>								
1910	4	3	4	41	1	4	31	1
1911	81	8	3	34	1	7	49	11
1912	61	2	1	75	31	7	37	1
1913	53	2		4	44	3	71	16
1914	70	6		64	64		26	9
1915	85		1	30	46	4	35	18
Total	354	21	11	208	143	21	169	57
<i>Series II Gastric and Duodenal Pile</i>								
1910	13	4	1	10	0	1	0	1
1911	24	2	2	1	1		0	1
1912	15		1	12	1	1	0	1
1913	18			14	11	1	6	1
1914	21	2		18	17	1	1	1
1915	9	1		4	6		0	1
Total	90	14	4	72	35	4	53	10

Table XIX shows patient reaction to milk and cream immediately after time of the stomach after administering milk and cream.

One patient noted slight transient upper abdominal distress. Another complained of nausea, weakness, and had marked diarrhoea. The difficulty

TABLE XVII. PATIENTS IN FOOD THERAPY

YEAR	TOTAL NOS.	HEALD	REFUSED	0 FOL.	RETO	STRICTLY ALL.	MILK	DOC.	SWISS FOODS	JEAN FOODS
Series I Duodenal (for Gastric and/or Ulcer)										
1940	4	3	1	31	5	38	1		6	
1941	51	5	3	48		34		3	13	1
1942	61		1		2	53	3		11	
1943	57	2		4	4	43	9		7	
1944	60	6		54	2	31	9	3	3	
1945	53		1	50		19	7		6	
Total	226	23	11	192	14	211	11		62	1
Series II Gastric and Pyloric Ulcers										
1940	16	4	1	1	1	9	1		3	1
1941	14	2	2	10	0	10			2	
1942	18	2	1	15	0	1	6		3	
1943	16	2	0	14	1	11	2			1
1944	21	2	0	19	0	18	1		2	
1945	9	1	0	8		9				
Total	90	14	4	72	1	70	4		9	2

\*Of these 13 per cent (3 patients) had no dietary restrictions, except for simple foods; 33 per cent (7 patients) had no dietary restrictions, except for simple foods; 33 per cent (7 patients) had no dietary restrictions, except for simple foods; 33 per cent (7 patients) had no dietary restrictions, except for simple foods.

In Series II of the patient followed, 136 per cent of the patients ate all foods with no restriction. 236 per cent had no dietary restriction except for single food and 1 per cent observed dietary restrictions for multiple foods.

It was found that a considerable number of patients were not drinking milk since the operation. The question arose as to whether this was due to an intolerance to milk or merely a dislike because of long usage in medical regimen prior to surgery. Symptoms of intolerance to milk were nausea, feeling of fullness, upper abdominal distress, and vomiting in some cases.

Table XVIII shows patients' tolerance to milk in Series I and II.

Of the 364 patients followed in the two series, 94 patients reported they did not drink milk postoperatively. Twenty-seven patients stated they did not drink milk preoperatively and postoperatively. A definite aversion to milk was noted in 6 patients, or 16.9 per cent. These individuals reported no distress from milk, but had acquired a distaste for it from long usage as a part of the medical regimen. The remaining 37 or 11 per cent did not drink milk postoperatively because they were intolerant to it.

Eleven patients were studied who stated they were intolerant to milk. A Relford duodenal tube was passed into the stomach and positioned under fluoroscope so that the end of the tube lay just within the gastric pouch. Then 200 cc. of 31 per cent butterfat milk was placed in an ordinary intravenous flask which was completely covered to prevent the patient from knowing what was being administered. This was run in rapidly to simulate the patient's drinking milk under ordinary circumstances.

TABLE XVIII. TOLERANCE TO MILK

YEAR	TOTAL (CASES)	DIED	REF. AND FOR POSTOP	DIED	USE OF MILK PREOP		USE OF MILK POSTOP		POSTMORTEM STUDIED
					PREOP YES	POSTOP YES	YES	NO	
Series I Duodenal Ulcer Gastrojejunal Ulcer									
1940	4	1	4	41	17	4	2	13	1
1941	31	5	3	49	37	9	29	11	
1942	87	2	1	74	51	7	37	1	7
1943	57			4	44	3	77	16	4
1944	70	6		54	54		74	20	9
1945	57		1	30	4	4	33	13	7
Total	236	15	11	244	160	1	190	10	31
Series II Gastric and Pyloric Ulcers									
1940	15		1	10	9	1	6	1	1
1941	26		3	1	9	1	7	3	
1942	13		1	1	1		9	1	
1943	16			14	13	1	8	6	
1944	21	3		19	17	1	13	3	1
1945	9	1		8	8		5	3	
Total	80	14	4	74	65	4	57	19	4

Table XIX shows patients' reaction to milk and ream after emptying time of the stomach after administering milk and ream.

One patient noted slight transient upper abdominal distress. Another complained of nausea, weakness, and had marked diaphoresis. The difficulty



In Series II of the patients followed, 73.6 per cent of the patients ate all foods without an restriction. 16 per cent had no dietary restriction, except for single food and per cent observed dietary restrictions for multiple foods.

It was found that a considerable number of patients were not drinking milk since the operation. The question arose as to whether this was due to an intolerance to milk or merely a dislike because of long usage in medical regimen prior to surgery. Symptoms of intolerance to milk were nausea, feeling of fullness, upper abdominal distress, and vomiting in some cases.

Table XVIII shows patients' tolerance to milk in Series I and II.

Of the 364 patients followed in the two series, 94 patients reported they did not drink milk postoperatively. Twenty-seven patients stated they did not drink milk preoperatively and postoperatively. A definite aversion to milk was noted in 5 patients, or 16.9 per cent. These individuals reported no distress from milk but had acquired a distaste for it from long usage as part of the medical regimen. The remaining 37 or 11 per cent did not drink milk postoperatively because they were intolerant to it.

Eleven patients were studied who stated they were intolerant to milk. A Rhoft duodenal tube was passed into the stomach and positioned under fluoroscope, so that the end of the tube lay just within the gastric pouch. Then 900 cc of 3½ per cent butterfat milk was placed in an ordinary intravenous flask which was completely covered to prevent the patient from knowing what was being administered. This was run in at all times to simulate the patient's drinking milk under ordinary circumstances.

TABLE XVIII TOLERANCE TO MILK

YEAR	TOTAL CSES	DEAD	NO FOOD OR LIPID	MILK LIPID		NO OF MILK POSTOP		DEATHS DUE TO TUBERCULOSIS	
				YES	NO	YES	NO		
Series I Duodenal Ulcer, Gastritis, and Ulcer									
Total	4	1	4	41	17	4	5	13	1
1911	31	5	1	40	17	3	9	11	
1912	1		1	34	51	7	17	1	
1913	57	2		49	44	3	11	16	9
1914	80	6		34	54		22	7	9
1915	57		1	30	46	4	13	15	7
Total	129	1	11	188	168	1	190	11	11
Series II Gastric and Pyloric Ulcers									
1916	15		1	10	9	1	9	1	1
1917	14			1	1		7	2	
1918	13		1	1	1		9	3	
1919	16	2		14	13	1	4		
1920	1	3		13	17	1	15	1	1
1921	9	1		8	9		4	3	
Total	68	14	4	56	64	4	53	16	4

Table XIX shows patients' reaction to milk and cream and emptying time of the stomach after administering milk and cream.

One patient noted slight transit of upper abdominal distress. Another complained of nausea, weakness, and had marked diaphoresis. The difficulty

TAKI VILL POSTNETS FOR TOURS CE

CR	TOTAL ADULTS	HEAD	BL/CR	FOU- LO FO	FE STRENGTH	ALL	Ren I Deadened Filter Gastrointestinal Filter	MILK	CHOC	ANALYST	APK CORR	FIELD MOODS
137	1	1	4	41	3	10		1				
1341	61	5	3	41	2	74			3	13	1	
136	61	2	1	50	1	31		7		31		
1311	57			4	4	13		9		7		
1344	60			34	7	31		9	3			
1345	83	2	1	20		19				8		
Total	326	34	11	229	19	271		31		62	1	
1340	18	4	1	1	1	9		1		3	1	
1341	74		2	10	0	10				3		
134	16	2	1	1	1	12				3		
1345	16		9	14	1	13						1
1311	31	7		1		1		1				3
1345	9	1	0	8		8						
Total	160	14	4	141	4	88		4		6	1	

NOTE: These are single adults per herd (131 in units) and all milk (134 in units) observed. All 6 per cent (83 patients) had no dietary restrictions except for those 73 per cent (13 patients) who all (milk) had any restriction. 23 6 per cent (17 patients) had no dietary restrictions except for those 13 patients who all (milk) had any restriction or multiple milk.

Carbohydrate particularly in form of desserts, was most common food hated with which patients had difficulty. Sweets were not tolerated in 61 or 16 per cent, of the patients. Symptoms listed were distress, nausea and vomiting in some cases.

Eleven patients were investigated for intolerance to sweets by putting 30 Gm of glucose in 400 c.c. of water into the stomach. This was administered in the same manner as was done with milk. Blood sugars were taken for fast and values at 15 minute interval for the first hour then at one-half hour intervals for the remainder of the two and one-half hour period. Only one patient complained of any distress. He had slight nausea during the first fifteen minutes of the test.

The blood sugar values in the 11 patient showed a rapid and often an abnormally high increase. They also showed abnormally low values at two to two and one-half hours. The time of maximal increase of blood sugar was found to be at thirty minutes in 7 of the cases, forty five minutes in 3 cases and one hour in 1 case.

TABLE XX. GLUCOSE TOLERANCE TEST

HOSPITAL NO.	SEX	REACTION TO GLUCOSE	0	15 MIN.	30 MIN.	45 MIN.	1	1½	2	2½
74132 (R) (m)	Male	Duodenal ulcer	None	80	179	184	151	141	134	75 68
74134 (R) (f)	Female	Duodenal ulcer	None	125		164		463	174	145
74134 (R) (m)	Male	Duodenal ulcer	Slight nausea 15 min.	65	181	191	150	90	59	60
74138 (R) (m)	Male	Duodenal ulcer	None	85	171	180	155	130	90	71
74140 (R) (f)	Female	Duodenal ulcer	None	71	475	273	289	500	170	87
74141 (R) (m)	Male	Duodenal ulcer	None	61	163	118	119	133	40	44
74146 (R) (m)	Male	Duodenal ulcer	None	50	116	183	182	61	44	
74148 (R) (f)	Female	Gastric	None	116	243	303	227	113		104 105
74151 (R) (m)	Male	Duodenal ulcer	None	116	220	255		266	136	167
74151 (R) (m)	Male	Duodenal ulcer	None	85	177	214	249	187	163	77 68
74153 (R) (m)	Male	Duodenal ulcer	None	103		493	149	63	79	77



lasted for about fifteen minutes and gradually disappeared. This is the only case observed here where symptoms elicited were comparable to those of dumping syndrome.

In nine patients no distress was noted during the period of administration and for one half hour following. It would appear that the psychological factor might play a part in patients who were intolerant to milk.

Four patients were given 50 c.c. of 30 per cent butterfat cream in the same manner as that described for milk, and no distress was noted in any case.

In five patients there was moderate increase in emptying time of the stomach after the administration of milk.

In the three of the four patients who were given cream, there was an appreciable delay in the emptying time of the stomach.

TABLE XIX. TOL- to MILK in COW

HOSPITAL NO., NAME	DIAGNOSIS	HEIGHT OF SUBJECT	REACTION TO MILK	CONTROL EMPTYING TIME (MIN.)	AFTER MILK (MIN.)	REACTION TO CREAM	EMPTYING TIME AFTER CREAM (MIN.)
118118 (T.H.) (F)	Duodenal ulcer	143 cm	None	14	23		
111111 (F.P.) (M)	Duodenal ulcer	143 cm	None	13	18	None	41
111111 (O.M.) (M)	Duodenal ulcer	173 cm	Mild transient postprandial distress	1	18		
111111 (J.T.) (M)	Duodenal ulcer and gastric	153 cm	None	12	18	None	26
111111 (E.H.) (M)	Duodenal ulcer	161 cm	None	10	25		
111111 (H.P.) (M)	Gastric	150 cm	None	14	14	None	30
111111 (B.H.) (F)	Duodenal ulcer	156 cm	None	1	13		
111111 (F.O.W.) (M)	Duodenal ulcer	143 cm	None	16	14		
111111 (J.H.) (M)	Duodenal ulcer	150 cm	None	11	23		
111111 (J.W.) (F)	Duodenal ulcer	151 cm	None	14	14		
111111 (A.H.) (M)	Gastro jejunal	151 cm	Deep, frequent, persistent, cephalic, tachycardia, and nausea	3	23	None	41

\*This barium mixture of 150

cc and 1 oz of barium

Carbohydrate, particularly in form of desserts, was most common food listed with which patients had difficulty. Sweets were not tolerated in 61 or 16 per cent, of the patients. Symptoms listed were distress, nausea and vomiting in some cases.

Eleven patients were investigated for intolerance to sweets by putting 50 Gm of glucose in 200 c.c. of water into the stomach. This was administered in the same manner as was done with milk. Blood sugars were taken for fasting values at 15 minute interval for the first hour then at one-half hour intervals for the remainder of the two and one-half hour period. Only one patient complained of any distress. He had slight nausea during the first fifteen minutes of the test.

The blood sugar values in the 11 patients showed a rapid and often an abnormally high increase. They also showed abnormally low values at two to two and one-half hours. The time of maximal increase of blood sugar was found to be at thirty minutes in 7 of the cases, forty five minutes in 3 cases and one hour in 1 case.

TABLE XX. GLUCOSE TOLERANCE TEST.

HOSPITAL NO.	NAME	REACTIO TO GLUCOSE	5 MIN.	15 MIN.	30 MIN.	45 MIN.	1 HR.	1½ HR.	2 HR.	2½ HR.
10052 (R.I.) (m)	Duodenal ulcer	None	80	179	168	181	148	124	73	80
10056 (R.K.) (f)	Duodenal ulcer	None	123		164		162	174		148
10114 (R.P.) (m)	Duodenal ulcer	Slight nausea 15 min.	80	131	162	140	60	39		68
10126 (R.P.) (m)	Duodenal ulcer	None	63	171	160	133	130	89	71	
10146 (P.R.) (f)	Duodenal ulcer	None	71	108	273	259	100	150	87	
10151 (J.B.) (m)	Duodenal ulcer	None	1	103	113	116	112	40	44	
10159 (J.R.) (m)	Duodenal ulcer	None	80	149	138	151	81	44		
10173 (R.R.) (f)	Gastric	None	110	223	303	227	119		104	172
10233 (E.H.) (m)	Duodenal ulcer	None	116	250	284		286	198	167	
10311 (E.D.) (m)	Duodenal ulcer	None	83	167	214	254	187	113	77	60
10343 (J.K.) (m)	Duodenal ulcer	None	103		283	149	83	79	77	

Two cases showed an increase over 210 mg per cent during the first fifteen minutes. In six of the cases the blood sugar was markedly increased.

In the hypoglycemic period there were four patients whose blood sugars were 66 mg per cent or lower. One had a blood sugar value of 39 mg per cent at the one and one-half hour period without experiencing any symptoms. No patients with low blood sugar values had symptoms.

From this small series of patients, it appears that there is no relation between blood sugar values and the occurrence of symptoms. No distress occurred in these patients from the ingestion of a 50 per cent glucose solution, although they claimed distress by carbonates.

Table XX shows the blood sugar values obtained.

#### POSTOPERATIVE ABILITY TO WORK

It has been stated that the patient should be capable of carrying on regular employment to warrant classification of a good result. In the study 341 cases were followed as to the patient's ability to work. Table XXI shows the postoperative ability to work according to sex, type of work, and year followed, for Series I and II respectively.

The type of work was divided into heavy, medium, and light for both sexes. These designations were set up according to work usually done by men and women. Males classified as doing heavy work were farmers, machinists, common laborers, and men whose occupations required expenditure of considerable physical exertion. Females employed in heavy manual labor outside of home particularly heavy farm chores were placed in heavy type classification.

Men employed in a managing or supervisory capacity, clerk in stores, or those whose jobs demanded considerable physical movement were classed in medium type work. Women doing their own housework or working as light domestics were also classified medium.

Men in executive desk positions, white collar workers, and those doing sedentary work were classified as light. Women doing light household tasks, secretaries, and office personnel were classified as doing light work.

Of the 341 cases in which follow-up study was done 283 were males and 58 females.

Table XXI A indicates the total patient followed in the two series according to their ability to work and the type of work they are doing.

TABLE XXI A

	MALES (283)		FEMALES (58)	
	Heavy	Med.	Med.	Light
Heavy type work	133	218		282
Medium type work	60	215	23	238
Light type work	44	135	16	150
Not working	20	71		
Unable to work	4	14	1	17
Total	261	654	40	450

Of the 94 males not working only 4 were unable to work because of difficulties relating to their postoperative conditions. The remaining 90 patients were not working because of a condition not related to their operation such as pulmonary tuberculosis, postmeningitis, asthma, arthritis, syphilis, lateral sclerosis, psychosis, blindness, senility or retirement.

TABLE XVI. POSTOPERATIVE ABILITY TO WORK &amp; ODDS TO BEY

CASE	TOTAL CASES	A						ODS	REASON
		BEAD	RECORD	FOLLOWED	LIGHT	WEEKS	IN HEAVY		
Group I Dorsal & Thoracic									
1	1	2	3	25	3	1	7	4	1 Blind 1 Retired 1 Unable to work
2	37	7	6	16	5	1	16	4	1 Pulmonary Tbc 1 Bronchitis and asthma
3	61	4	7	42		7	15	3	1 Postmeningitis 1 Unable to work 1 Old age
4	46			35		1	5	1	1 Arthritis
5	49	1	4	34	11	11	19	1	1 Retired
6	44			30	4	10	18	6	1 Blind 1 Post bone 1 (X) syphilis 1 Unable to work 1 Lateral sclerosis
7	71	16	5	27	19	44	13	21	
8		1		5	1	1		1	1 Unable to work
9	1	1	1	1		1			
10					4	4	1		
11	7		1			4			
12	11				4		1		
13	1			10	5	5			
14	55	7		46	15	76	4	1	
15	256	1	90	171	51	7	127	13	
Group II Lumbar & Sacral									
16			1			1	4	1	1 Senility
17	11			10		1	7		
18	11	1				3	4	1	1 Syphilis
19	15		1					1	1 Arthritis 1 mental depression
20	1	2	1	15	1	4	10		
21	7	1			2	5	1		
22	72	6	7	64	5	1	31	1	
23		4							
24									
25	1	1	1		1	1			
26	4			4		4			
27									
28									
29	1	3	1	15	1	6			
30	16	14	4			25	14	4	

Two cases showed an increase over 210 mg per cent during the first fifteen minutes. In all of the cases the blood sugar was markedly increased.

In the hypoglycemic period there were four patients whose blood sugars were 66 mg per cent or lower. One had a blood sugar value of 39 mg per cent at the one and one-half hour period without experiencing any symptoms. No patients with low blood sugar values had symptoms.

From this small series of patients, it appears that there is no relation between blood sugar values and the occurrence of symptoms. No distress occurred in these patients from the ingestion of a hypertonic glucose solution, although they claimed distress by carbohydrates.

Table XX shows the blood sugar values obtained.

#### POSTOPERATIVE ABILITY TO WORK

It has been stated that the patient should be capable of carrying on regular employment to warrant classification of a good result. In the study 341 cases were followed as to the patient's ability to work. Table XXI shows the postoperative ability to work according to sex, type of work, and year followed, for Series I and II respectively.

The type of work was divided into heavy, medium, and light for both sexes. These designations were set up according to work usually done by men and women. Males classified as doing heavy work were farmers, machinists, common laborers, and men whose occupations required expenditure of considerable physical exertion. Females employed in heavy manual labor outside of home, particularly heavy farm chores, were placed in heavy type classification.

Men employed in a managing or supervisory capacity, clerk in stores, or those whose jobs demanded considerable physical movement were classified as medium type work. Women doing their own housework or working as light domestics were also classified medium.

Men in executive desk positions, white collar workers, and those doing sedentary work were classified as light. Women doing light household tasks, secretaries, and office personnel were classified as doing light work.

Of the 341 cases in which follow-up study was done 203 were males and 138 females.

Table XXI A indicates the total patients followed in the two series according to their ability to work and the type of work they are doing.

TABLE XXI A

	MALES (203)		FEMALES (138)	
	N	PER CENT	N	PER CENT
Heavy type work	133	51		10.1
Medium type work	80	21.8	25	60.3
Light type work	44	13.3	10	27.5
Not working	20	7.1		
Unable to work	4	1.4	1	1.7
Total	281	100	36	100

The average weight of the resected specimens in the female patient who were not obstructed was significantly smaller than in the males in the cases of duodenal and gastric ulcer. In the obstructed patients, this relationship was not uniformly seen in all the series.

10 Achlorhydria was found following the Group III operation in Series I as follows: 85.6 per cent of cases were achlorhydric: 85 per cent males, and 90 per cent females. In Series II achlorhydria was found in 88 per cent of the cases: 88 per cent males, and 89 per cent females.

Achlorhydria was found in Group IV A operation in Series I as follows: 84.8 per cent of cases were achlorhydric: 89.7 per cent males, and 100 per cent females.

In Group IV operation, achlorhydria was found in 71 per cent of the cases. It was shown that achlorhydria was more easily obtained in females than in males.

11 Groups III and IV A were the standard operative procedures used in the surgical treatment of the cases. The Group IV operation was discontinued early in 1941 since it was quickly realized this operation was unsatisfactory. Of the patients who had Group IV operation 50 per cent were unsatisfactory. There were only six patients followed with this type operation.

Patients who had Group III operation in Series I revealed a favorable result in 96.6 per cent of the cases. The unsatisfactory result in this Series was 3.4 per cent. The recurrence rate was found to be 8.6 per cent.

In patients who had Group IV A in Series I a favorable result occurred in 98.9 per cent of the cases. The unsatisfactory result of 1.8 per cent included one recurrent ulceration. The recurrence rate in Series I with Group III and IV A operation was 1 per cent.

In Series II, a favorable result was obtained in 97.3 per cent of the patients. There were no recurrent ulcerations in this Series.

12 A favorable result was shown in 96 per cent of the males and 99.7 per cent of the females in Series I. In Series II a favorable outcome was shown in 96.7 per cent of the males and 100 per cent of the females.

13 No appreciable difference was noted in results between obstructed and nonobstructed patients.

14 Of the 51 patients followed seven years, hemoglobin values were obtained in 40 cases. Normal hemoglobin was noted in 100 per cent of the males and 83 per cent of the females. Only one case of severe anemia, which did not respond to iron therapy was encountered.

15 There was a total of 384 patients followed in Series I and II with regard to postoperative digestive difficulties. There were no digestive difficulties whatever in 311 or 86 per cent. Minor symptoms were found in 37 or 10 per cent and 16.4 per cent had multiple complaints.

16 There were 8 per cent of the patients who complained of symptoms of the so-called dumping syndrome. In no case were the symptoms of a severe degree.

The one female reported in Table XXIA unable to work had a recurrent ulcer following a Group IV operation.

It was found that the majority of patients who were doing light work returned to their employment in six to seven weeks. Those doing medium type work returned in approximately two to two and one-half months. With the exception of a few cases, the majority of patient returned to heavy type work in three months.

#### SUMMARY

1. We have followed what we believe are the criteria for a satisfactory operation for peptic ulcer.

First effective reduction of gastric secretion must be accomplished. This requires at least a 75 per cent resection of the stomach with excision of the entire lesser curvature and antrum.

Second, the anastomosis with the jejunum must be made in such a manner that the proximal duodenal-jejunal loop is as short as possible. This is possible only if a retrocolic anastomosis is performed.

Finally removal of the ulcer bearing area in the duodenum is not important so long as the antral mucosa is excised.

3. In this investigation 410 patients consecutively operated upon for peptic ulcer were considered. The study included all the patients treated from January 1, 1940, to July 1, 1945. Patients were followed by questionnaire and clinical examination in the outpatient department. Investigation covered the state of health of the patient postoperatively. The patients investigated and evaluated were followed for at least six years, and some seven years. They were classified postoperatively into four categories, namely, excellent, good, satisfactory and poor.

3. The cases were divided into two series. Series I consisted of 326 cases in which the problem was that of duodenal ulcer. In Series II there were 90 cases with ulcerations on the gastric side of the pylorus.

4. In the complete series there were 343 males and 73 females, indicating a ratio of 4.6 to 1.

5. The average age of patient of Series I was found to be 45.8 years. In Series II the average age was 54.7 years.

6. The average duration of symptoms shown in each of the series was 12.9 years in Series I and 8.4 years in Series II.

7. Pain occurred as a symptom in 96 per cent of the cases. In 20 per cent of the patients, pain occurred as the only symptom. Hemorrhage appeared as a symptom in 51.6 per cent and obstruction was present in 22.3 per cent.

8. The over-all mortality of the patients operated upon was 4.5 per cent. This included the seven cases of emergency operations for acute hemorrhage. Mortality for elective surgery was 3 per cent.

9. The average weight of the resected specimen in Series I in the non-obstructed patients was 187.23 Gm. and the average weight in the obstructed patients was 248.14 Gm. In Series II the average weight of the specimen in the nonobstructed patients was 207.3 Gm. and in the obstructed 254 Gm.

The operation as practiced here for peptic ulcer has resulted in only three recurrences a recurrence rate of less than 1 per cent. The mortality in elective operations was 3 per cent.

Subtotal gastric resection has been shown at this time to be an eminently satisfactory method of affording a very favorable result. Until other means of treatment are developed which will produce a more satisfactory result, subtotal gastrectomy will continue to be the best approach to the problem of peptic ulcer.

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17 There were 364 patients followed in Series I and II with regard to quantitative food intake. Of these 44 patients, or 87 per cent enjoyed three regular meals. 9 patients, or 6 per cent ate three regular meals plus supplemental feedings and 11 patients, or 65 per cent ate frequent small feedings.

18 Of the 364 patients followed in Series I and II regarding food intolerance it was found that 60.8 per cent were able to eat all foods without restriction; 34.7 per cent were able to eat regular diet but had difficulty with a single food and 4.4 per cent observed dietary restrictions for multiple foods.

19 Ninety-five patients reported they did not drink milk postoperatively; 16.9 per cent of the patients did not drink it because they had acquired a taste for it from long usage as part of the medical regimen.

In 11 patients studied for intolerance to milk one patient had slight distress and another had symptoms quite typical of the dumping syndrome following the administration of milk.

In a small series of cases studied for intolerance to cream no distress was noted.

It would appear that some intolerance to milk and cream might be explained on a psychologic basis.

Intolerance to sweets was noted in 16.7 per cent of the cases. Eleven patients were studied for intolerance to sweets by administration of glucose into the stomach and the simultaneous determination of blood sugars. Blood sugar values obtained showed rapid initial rise within the first 30 minutes. Abnormally low values were obtained at two and one-half hours.

20 On investigation of the work record of the patients, it was found that 91.5 per cent of the males were engaged in regular employment at the present time. 7.1 per cent were not working because of a condition not related to the operation or were retired and 1.4 per cent were unable to work because of difficulties relating to the postoperative condition.

Of the females, 98.3 per cent were engaged in regular employment at the present time; and one patient 1.7 per cent, was not working because of recurrent ulcer.

#### CONCLUSION

It appears from this follow-up investigation and evaluation that the Group III and IVA operation indicated gratifying number of favorable results. The majority of patients have been freed from the disease and are not threatened with constant danger of complication and are restored to a more normal way of living. They are able to enjoy life without observing dietary restrictions, and to resume gainful and useful employment.

There were a small number of patients who although benefited by the operation and enjoying fairly good health reported minor difficulties. None of these difficulties interfered with the patient's way of living, and were not severe enough to warrant concern. All of the patients were found to have made very good adjustment.

The operation as practiced here for peptic ulcer has resulted in only three recurrences, a recurrence rate of less than 1 per cent. The mortality in elective operations was 3 per cent.

Subtotal gastric resection has been shown at this time to be an eminently satisfactory method of affording a very favorable result. Until other means of treatment are developed which will produce a more satisfactory result, subtotal gastrectomy will continue to be the best approach to the problem of peptic ulcer.

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# CONCLUSION

It appears from this follow-up investigation and evaluation that the Group III and IVA operations indicated a gratifying number of favorable results. The majority of patients have been freed from the disease, are not threatened with constant danger of complications, and are restored to more normal ways of living. They are able to enjoy life without observing dietary restrictions, and to resume gainful and useful employment.

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# SURGERY

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## Original Communications

### THE PROBLEM OF THE SOLITARY LUNG TUMORS

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DURING the past decade the use of roentgenography has become more widespread than ever before. In particular roentgen examination of the thorax in apparently normal individuals has become one of the major factors in preventive medicine. It is for this reason that the clinician is more frequently confronted with diagnostic chest problems in people who profess no subjective symptoms. During World War II every member of the Armed Forces had a roentgen examination of the thorax on induction into the service and again on separation from the service. In addition to this many thousands of young people throughout the country are subject to chest examinations before being accepted at universities or for employment. It is among these apparently normal, healthy people that the occasional solitary shadow or spot is discovered on an otherwise normal lung field. The diagnosis and the management of these asymptomatic lesions may constitute a very real problem since history and physical findings are frequently noncontributory. It seems apparent that the incidence of these particular diagnostic problems will not subside as there is every indication that the widespread use of roentgenography will continue. As more roentgenograms of the thorax are made in apparently healthy individuals, an increasing number of unsuspected lesions of the lung will be detected.

The clinical management of the apparently normal individual who has an undiagnosed solitary lesion in the lung is frequently difficult. In past years an accepted procedure in the management of these patients has been observation over varying periods of time. However the value of clinical observation alone varies tremendously with the conscientiousness of the clinician and the fundamental intelligence and the cooperation of the patient. It is for these reasons that the fate of the majority of the so-called tumors of the chest is unknown. We may assume that the majority of these lesions were probably benign other wise the patients would likely re-establish contact with their physicians.

In the past decade there has been continued improvement in surgical and anesthesia techniques and the problem of elective exploration of the thorax has

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**D**URING the past decade the use of roentgenography has become more widespread than ever before. In particular roentgen examination of the thorax in apparently normal individuals has become one of the major factors in preventive medicine. It is for this reason that the clinician is more frequently confronted with diagnostic heat problems in people who profess no subjective symptoms. During World War II every member of the Armed Forces had a roentgen examination of the thorax on induction into the service and again on separation from the service. In addition to this many thousands of young people throughout the country are subject to chest examinations before being accepted at universities or for employment. It is among these apparently normal, healthy people that the occasional solitary shadow or spot is discovered on an otherwise normal lung field. The diagnosis and the management of these asymptomatic lesions may constitute a very real problem since history and physical findings are frequently noncontributory. It seems apparent that the incidence of these particular diagnostic problems will not subside as there is every indication that the widespread use of roentgenography will continue. As more roentgenograms of the thorax are made in apparently healthy individuals, an increasing number of unsuspected lesions of the lung will be detected.

The clinical management of the apparently normal individual who has an undiagnosed solitary lesion in the lung is frequently difficult. In past years an accepted procedure in the management of these patients has been observation over varying period of time. However the value of clinical observation alone varies tremendously with the conscientiousness of the clinician and the fundamental intelligence and the cooperation of the patient. It is for these reasons that the fate of the majority of the watched tumors of the chest is unknown. We may assume that the majority of these lesions were probably benign, otherwise the patients would likely re-establish contact with their physicians.

In the past decade there has been continued improvement in surgical and anesthetic techniques and the problem of elective exploration of the thorax has

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been greatly simplified. Ten years ago a thoracotomy was looked upon in most communities as a hazardous procedure and the presence of a benign tumor did not justify such a heroic operation. At the present time, however, exploratory thoracotomy can be performed by competent personnel with an expected mortality rate of less than 1 per cent. Consequently exploration of the thorax for the purpose of tissue biopsy or extirpation of a benign tumor is a commonplace accepted procedure today.

As more chest surgery has been performed in recent years, we have had greater opportunity to confirm our clinical and roentgenologic diagnoses. The purpose of this paper is to present a representative series of cases that were observed over a period of eighteen months in the department of thoracic surgery at the Walter Reed General Hospital. These case histories have been carefully selected and are presented with one purpose in mind. It is our belief that accurate preoperative diagnosis of an asymptomatic lung tumor is uncertain and, in most cases, impossible to make with the facilities that are generally available. Each of the twenty-four patients who are to be reported upon had a roentgen examination of the chest during a routine physical examination. In each case a round pulmonary lesion was discovered and in every case the lesion was completely asymptomatic. All of these patients were hospitalized for a short period of time and thorough examinations were performed in an effort to make a concrete clinical diagnosis. No patient is included in this series who had an unexplained cough, fever, hemoptysis, chest pain, weight loss, or localizing symptom that could be attributed to a primary or metastatic lung tumor. Each of these patients was hospitalized for an unrelated condition—five cases of the solitary lung tumor that had been discovered on an induction or a separation roentgenogram. The lesion under suspicion was in every case solitary and asymptomatic. Each of these patients was presented at The Tumor Board Conference or Thoracic Surgery Conference before operation. It is very interesting that there was never complete unanimity of opinion among the clinicians and radiologists who attended these conferences as to the specific diagnosis in each case. It is of more interest, however, that despite the wide variety of impressions which were proffered, all were considered benign tumors before operation. However, operation was advised to each of these twenty-four patients on the simple premise that diagnosis without tissue biopsy is only conjecture. All twenty-four patients agreed to surgical intervention and in each case a thoracotomy was performed. In this series of operative procedures both the mortality and the morbidity rates were zero. We feel that this group of patients is a representative one and that these findings should be presented to demonstrate the difficulty in establishing a diagnosis in the presence of solitary asymptomatic lung tumor without an actual tissue biopsy.

#### CASE HISTORIES

The inclusion of twenty-four case presentations in this discussion is not feasible, nor is it necessary. We have selected ten clinical abstracts and illustrations that are representative of the group. Although each case history has been condensed in the interest of brevity, it is understood that each of these pa-

TABLE I. PREOPERATIVE FORM TO OF CASE HISTORIES INCLUDED IN THE SERIES

CASE NO.	AGE YR.	PREOPERATIVE DIAGNOSIS	POSTOPERATIVE DIAGNOSIS	PROCEDURE	MORBIDITY	DATE
1	57	Tuberculosis	Tuberculosis	Wedge resection	0	1-/ 3/43
2	51	Tuberculosis	T. tuberculosis	Wedge resection	0	6/ 4/46
3	76	Tuberculosis	T. tuberculosis	R. L. L. lobectomy	0	
4	51	T. tuberculosis	Bronchiogenic carcinoma	L. L. L. lobectomy	0	8/ 4/46
5	47	Undetermined	Histiocytoma	Wedge resection	0	7/ 4/45
6	51	Fibrous nod. w.	Metastatic adenocarcinoma	R. U. L. lobectomy	0	9/16/46
	75	Bronchiogenic cyst	L. lymphosarcoma	Excision	0	10/15/46
7	32	Bronchiogenic cyst	Bronchiogenic cyst	R. U. L. lobectomy	0	9/ 8/46
8	4	Neurofibroma	Neurofibroma	Excision	0	7/ 5/46
10	38	Bronchiogenic cyst	Neurofibrosarcoma	1. Frexion Black excision of heart wall	0	7/10/46 7/ 1/46
11	46	Bronchiogenic cyst	Carcinoma lymph gland	Biopsy	0	10/16/45
12	78	Bronchiogenic cyst	Bronchiogenic cyst	Excision	0	9/1-/44
13	47	Bronchiogenic cyst	Echinococcus cyst	R. U. L. lobectomy	0	5/ 8/45
14	37	Echinococcus cyst	Bronchiogenic cyst	Excision	0	11/ 8/44
15	44	Bronchiogenic cyst	Empyema	Reps. f. dia. phragm.	0	3/25/4
16	31	Bronchiogenic cyst	Bronchiogenic cyst	R. M. L. lobectomy	0	4/ 8/47
17	19	T. tuberculosis	Tuberculosis	Lingulectomy	0	5/20/47
18	6	Bronchiogenic carcinoma	T. tuberculosis	Wedge resection	0	3/25/4
19	24	Undetermined	D. ph. lymph. carcinoma	Reps.	0	4/11/4
20	31	Bronchiogenic cyst	Bronchiogenic cyst	Excision	0	4/ 8/47
21	19	Undetermined	Carcinoma lymph. gland	Excision	0	4/ 9/4
22	57	Tuberculosis	T. tuberculosis	Excision	0	1/ 8/47
23	19	Empyema	Bronchiogenic cyst	Excision	0	7/16/4
24	20	Undetermined	T. tuberculosis	Lobectomy	0	10/ 7/4

tients received as complete a clinical study as the resources of a modern general hospital would permit. The majority of accepted diagnostic adjuncts have been employed prior to surgical exploration.

CASE 1—A white patient, aged 57 years, was admitted to the Walter Reed General Hospital with diagnosis of possible bladder neoplasm accompanied by lung metastases. Complete gross excretory examinations revealed benign errors of the bladder which was removed transurethrally. Roentgen examination revealed rounded, solitary tumor of the basal 1 cm of the right lower lobe. After successful postoperative recovery the patient returned to general duty. Final diagnosis was tuberculosis.

CASE 2—A white patient, aged 31 years, was admitted to the Walter Reed General Hospital for treatment of a peritrophic ribitis of the humerus space. Roentgen or fluorographic examination of the chest revealed solitary lesions in the left lower lobe that were not present on roentgenogram made four years earlier. There were no impressive irritative effects on pulmonary tissue. The preoperative impression was benign tumor, probably tuberculosis. Exploratory thoracotomy was performed on June 1, 1946, and a tumor removed by edge resection of the left lower lobe. The patient had a successful recovery following the operation and was discharged from the hospital. Final diagnosis was tuberculosis.

CASE 3—A white patient, aged 76 years, was admitted to the Walter Reed General Hospital in November, 1944. The dependent wife of an ex-serviceman. Roentgen examination revealed rounded mass in the dorsal division of the right lower lobe. The test to



been greatly simplified. Ten years ago a thoracotomy was looked upon in most communities as a hazardous procedure and the presence of a benign tumor did not justify such a heroic operation. At the present time, however, exploratory thoracotomy can be performed by competent personnel with an expected mortality rate of less than 1 per cent. Consequently exploration of the thorax for the purpose of tumor biopsy or extirpation of a benign tumor is a commonplace, accepted procedure today.

As more chest surgery has been performed in recent years, we have had greater opportunity to confirm our clinical and roentgenologic diagnoses. The purpose of this paper is to present a representative series of cases that were observed over a period of eighteen months in the department of thoracic surgery at the Walter Reed General Hospital. These case histories have been carefully selected and are presented with one purpose in mind. It is our belief that accurate, preoperative diagnosis of an asymptomatic lung tumor is uncertain and, in most cases, impossible to make with the facilities that are generally available. Each of the twenty-four patients who are to be reported upon had a roentgen examination of the chest during a routine physical examination. In each case a round pulmonary lesion was discovered and in every case the lesion was completely asymptomatic. All of these patients were hospitalized for varying periods of time and thorough examinations were performed in an effort to make a correct clinical diagnosis. No patient is included in this series who had an unexplained cough, fever, hemoptysis, chest pain, weight loss, or any localizing symptom that could be attributed to a primary or metastatic lung tumor. Each of these patients was hospitalized for an unrelated condition or because of the solitary lung tumor that had been discovered on an inclination of a separation roentgenogram. The lesion under suspicion was in every case solitary and asymptomatic. Each of these patients was presented at The Tumor Board Conference or Thoracic Surgery Conference before operation. It is very interesting that there was never complete unanimity of opinion among the clinicians and radiologists who attended these conferences as to the specific diagnosis in each case. It is of more interest, however, that despite the wide variety of impressions which were professed, all were considered benign tumors before operation. However, operation was advised to each of these twenty-four patients on the simple premise that diagnosed without biopsy is only conjecture. All twenty-four patients agreed to surgical intervention and in each case thoracotomy was performed. In this series of operative procedures both the mortality and the morbidity rates were zero. We feel that this group of patients is a representative one and that these findings should be presented to demonstrate the difficulty in establishing a diagnosis in the presence of solitary asymptomatic lung tumor without an actual tissue biopsy.

#### CASE HISTORIES

The inclusion of twenty-four case presentations in this discussion is not feasible, nor is it necessary. We have selected ten clinical abstracts and illustrations that are representative of the group. Although each case history has been condensed for brevity it is understood that each of these pa-

Case 4—A white male aged 51 years was transferred to the Walter Reed General Hospital for study of an undiagnosed lung tumor. The solitary lesion was demonstrated on routine roentgen examination. There was no additional evidence of metastatic disease. The tumor was localized to the left lower lobe and was thought to be tuberculous. On Aug. 10, 1946, thoracotomy was performed and the lesion removed by left lower lobectomy.

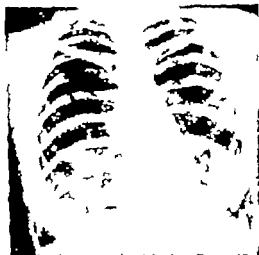


Fig. 3 (Case 4).—Note central position and basal level of tumor of left lower lobe. This tuberculous had been under observation for 5 years prior to lobectomy.



Fig. 4 (Case 5).—Tumor of left lower lobe which proved to be peripheral bronchioloalveolar carcinoma. The clinical impression before operation was tuberculous. There was no evidence of metastatic disease (after lobectomy).

lobectomy. After an uneventful recovery he again returned to general duty. The patient was last seen eighteen months after operation and appeared to be in excellent health. Final diagnosis: bronchioloalveolar carcinoma.

Case 5—A Negro male aged 47 years was inducted in the Army in August, 1942. Postmortem revealed primary epithelioid lesion in 1939 that was inadequately

Impression of the attending physician was tuberculosis and no treatment advised. At approximately one and one-half years later another roentgen examination of the chest was performed and there was marked change in the character of the solitary lesion. During this period of observation the lesion had increased in size and showed definite central calcification. The patient was transferred to the tuberculosis sanatorium and right pneumothorax was instituted. The roentgen films were reviewed several months later and presented for the first time at the Thoracic Surgery Conference at the Walter Reed General Hospital. Excisional surgery was recommended and the patient returned to the right lower lobe lobectomy performed. The patient has been discharged to her own care and is enjoying excellent health one year after operation. Final diagnosis was tuberculosis.



Fig. 1 (Case 1).—The tumor is located in the basal portion of the right lower lobe. The effluential impression of tuberculosis, as confirmed by surgical removal.

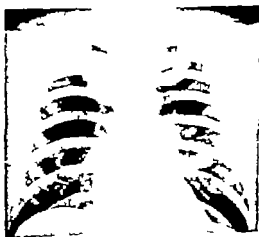


Fig. 2 (Case 2).—Asymptomatic tumor in the left lower lobe. Final diagnosis was tuberculosis.

CASE 4.—A white patient aged 51 years was transferred to the Walter Reed General Hospital for study of a diagnosed lung tumor. The solitary lesion was demonstrated on a routine roentgen examination. There were no additional subjects of study. The tumor was localized to the left lower lobe and was thought to be a bronchogenic carcinoma. On August 1, 1946, thoracotomy was performed and the lesion removed from the left lower lobe.

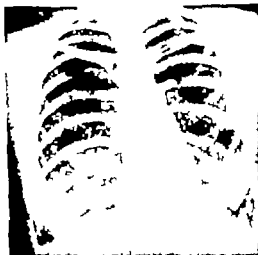


Fig. 2 (Case 3).—Note central extension and final level in tumor of right lower lobe. This tuberculous had been stable about same level for 10 years prior to lobectomy.



Fig. 3 (Case 4).—Tumor of left lower lobe. An apparent peripheral bronchogenic carcinoma. The clinical impression before operation was of a bronchogenic carcinoma. There was no evidence of metastatic disease, neither after lobectomy.

lobectomy. After several months in the office followed by general diet. The patient was last seen eighteen months after operation and appeared to be in excellent health. Final diagnosis: bronchogenic carcinoma.

CASE 5.—A Negro patient aged 41 years was inducted into the Army in August 1942. Past history revealed primary syphilis lesions in 1929 that was adequately

treated by medical and surgical. While on record date May 1944 the patient was hospitalized because of papular eruption of both palms surfaces and vesicular lesions throat. Serologic examination reported strong positive antistreptococcal therapy. At that time, complete examination of the right middle lobe. The impression of pulmonary carcinoma was entertained but the lesion showed no regression or change after treatment. The complete examination of the Walter Reed General Hospital confirmed the finding of the lesion but no specific diagnosis could be made. On July 4, 1944, the right thorax was explored and the tumor removed from the right middle lobe. The patient made an uneventful recovery and returned to duty. Final diagnosis: hamartoma.



Fig 5 (Case 5)—Lateral projection reveal solitary tumor in right middle lobe. Microscopic diagnosis follows our middle lobe lobectomy was hamartoma.

CASE 6—A male patient, aged 61 years, was reported from November 1944, with a black and annular lesion of the sigmoid colon. He was treated and an exploratory laparotomy of the bowel performed. The tumor was registered with the diagnosis of adenocarcinoma, with no regional metastasis. The other returned to duty and for period of six years.

of tuberculosis recommended during his time there as no apparent signs of tuberculosis. The chest X-ray and the sputum examination revealed no evidence of tuberculosis. At the recommendation of the Thoracic Surgery Conference an exploratory thoracotomy was performed on Sept 18, 1948. The lesion was easily removed from the right upper lobe and frozen section examination revealed the nodule as adenocarcinoma, metastatic from the large bowel. A right upper lobectomy was then performed. There was no evidence of other metastases in the right lung or mediastinum. The uneventful postoperative course was noted and the patient returned to his active service. Final diagnosis was adenocarcinoma metastatic from the large bowel.

CASE 7—A male patient, aged 49 years, was taken ill and hospitalized with the diagnosis of pneumonia while on overseas duty. Roentgen examination revealed shadow character typical of pneumonia which gradually resolved. Following resolution of the alleged pneumonia process neither abnormal shadow was discovered. The lesion was very old.

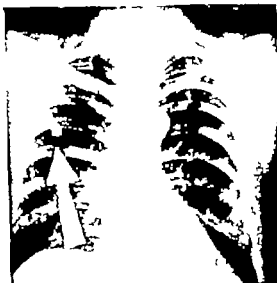


Fig. 6 (Case 6).—Roentgenogram appears normal except for solitary lesion of right upper lobe. Macroscopic diagnosis following right upper lobe lobectomy was adenocarcinoma, nests made from large nests. The patient is in good health fifteen months after surgery.



Fig. 7 (Case 7).—Lateral projection of thorax reveals solitary lesion which was presumed to be in the right upper lobe. The tumor was removed surgically and the pathologic diagnosis of lymphosarcoma established. This tumor was extrapulmonary, apparently arising from the mediastinum.

ected and bore no resemblance to the original process. After five months of observation the lesion showed no significant change although the patient was entirely free of symptoms. After the patient was transferred to the Walter Reed General Hospital physical examination was entirely normal except for the lesion which could be radiologically demonstrated in the right upper lobe. It was felt that this patient had a bronchogenic cyst that had probably become infected and produced superimposed pneumonia. Exploratory thoracotomy, October 1948, revealed an intrapulmonary solid tumor that probably arose from mediastinum. This solid mass effected recovery and has enjoyed excellent health since time of discharge one year ago. Final diagnosis was lymphosarcoma.

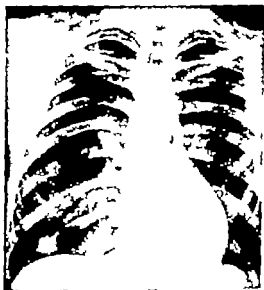


Fig 3 (Case 8) —Roentgen Aron Separation roentgenogram of the chest revealing an asymptomatic tumor in the right upper lobe. Postoperative diagnosis — bronchogenic cyst.

CASE 9—A hit patient, aged 21 years, was transferred from separation center to the Walter Reed General Hospital. Final physical examination was entirely normal except for the roentgen finding of solitary lung tumor. The lesion was located in the right upper lobe and was thought to be bronchogenic cyst. Exploratory thoracotomy was performed and it was necessary to perform right upper lobe lobectomy. Recovery was prompt and the patient was discharged from the hospital approximately one month after operation. Final diagnosis was bronchogenic cyst.

CASE 10—A white patient, aged 30 years, had roentgen evidence of intrathoracic tumor detected at an Aron Separation Center. The lesion appeared to be perfectly spherical and was about the size of tennis ball. A review of the radiative roentgenogram showed no evidence of the lesion. I was generally agreed by the members of the Tumor Board that the neoplasm was probably benign and represented bronchogenic cyst arising from the post lateral segment of the left upper lobe. An exploratory thoracotomy was performed on July 10, 1948, and lesion was arising from the chest wall and proved to be entirely extrapulmonary. Microscopic studies subsequently yielded the diagnosis of neurofibrosarcoma with microscopic capsule in place. A second operation was then performed and block excision of the chest wall performed. The patient withstood both operative procedures very well and has been discharged from the service. Final diagnosis was neurofibrosarcoma.



Fig 8 (Case 8).—Cross section of bronchovesicle cyst removed during exploratory thoracotomy.



Fig 9 (Case 8).—Xerothoracoma of the chest wall discovered on routine x-ray. Separation film. This tumor moved with respiration and was thus found to be intrathoracic.



CASE 13.—A white patient, aged 27 years, was hospitalized while on active duty with the continental limits of the United States. The chief complaint was acute sore throat. The patient rapidly recovered but further studies were ordered after routine admission roentgenogram revealed large circumscribed lesion in the right upper lobe. All physical findings were normal; however the Kahn and Wassermann tests were reported as strongly positive. There were no symptoms of any kind; past history revealed that the



FIG. 11



FIG. 12

FIG. 11 (Case 16).—Echinococcus cyst in right upper lobe discovered on routine hospital admission roentgenogram of chest.

FIG. 12 (Case 9).—Lateral view of echinococcus cyst in right upper lobe.

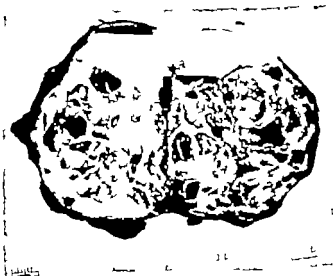


FIG. 13 (Case 20).—Gross section of bronchiogenic cyst removed during thoracotomy.

soldier had several years in England, North Africa, and Sicily. In May 1945, right upper lobe lobectomy was performed and the lesion identified as an echinococcus cyst. Recovery was complete and uneventful. Final diagnosis was echinococcus cyst.

#### COMMENT

Twenty-four case presentations do not constitute an impressive series of intrathoracic tumors. However, it must be emphasized that each of these cases has been selected from a much greater number because it conforms to these specific criteria:

1. The lesion was an incidental radiologic discovery.
2. The impression of a solitary lung tumor was based on the roentgen findings alone.
3. There were no symptoms or physical findings related to the tumor.
4. All lesions were considered benign neoplasms preoperatively.

Patients who had obvious chest wall or mediastinal tumors are excluded from this series. Likewise, no case is included in which the patient had a tumor amenable to bronchoscopic biopsy.

After a comprehensive study of the pulmonary tumors removed surgically at the Walter Reed General Hospital it was our opinion that ultimately tissue biopsy is the only diagnostic procedure of true value. Since most of the patients with pulmonary neoplasms have some symptoms of thoracic disease there is little question that surgical intervention is indicated in the majority of cases. Few conscientious clinicians would hesitate to ask for surgical opinion when a patient with complaints of cough, sputum, hemoptysis, fever, weight loss, and the like has roentgen evidence of a lung tumor. However, many doctors are reluctant to consider the patient with an asymptomatic lung tumor as a candidate for surgery. The belief that solitary round masses in the lung fields are relatively harmless entities is unfortunately a widespread medical opinion. The series of case histories presented in this paper demonstrates well the difficulty of establishing a diagnosis without tissue biopsy; this is particularly significant since the diagnostic facilities at hand were unlimited. It is of particular note that approximately 15 per cent of the tumors proved to be malignant neoplasms after adequate tissue studies were performed. This in itself justifies surgical exploration of every solitary tumor of the lung even though the patient is symptom free and the lesion has every indication of being benign.

A review of the cases presented (see Table I) discloses that seven of the tumors proved to be tuberculomas. Of the remaining seventeen, four lesions were malignant tumors. Again it is unfortunate that most doctors consider a tuberculoma an innocuous lesion if it is not accompanied with roentgen evidence of a diffuse parenchymal disease. Case 3 (see Figs. 1 and 4) illustrates one of the complications that may follow in an untreated patient. This tumor was observed for a period of almost two years while it progressed to central cavitation whereupon the patient's sputum demonstrated acid fast bacilli for the first time. The opinion that all tuberculomas should be excised is generally accepted by thoracic surgeons today. Experience has shown that the tuberculoma is

benign only in the sense that it does not undergo neoplastic degeneration the benignity of the lesion ceases there.

It must also be pointed out that the age incidence of the patients presented in this series is comparatively young. Since these people were seen in a military hospital during wartime the reason is self-evident. A comparable series in which the average patient age exceeded 50 years would probably show a higher incidence of malignant tumors, thereby emphasizing even more the importance of surgical exploration in the presence of an asymptomatic lung tumor.

#### CONCLUSIONS

With the continued increase in radiologic methods of diagnosis we can expect to see a greater incidence of asymptomatic intrathoracic neoplasms. The question will always arise in the mind of the clinician, is this tumor benign or malignant? From the experience gained in this series of twenty four cases we can assume the question can be answered only by tissue study of the entire lesion. Prolonged observation is always inconclusive and may prove disastrous in certain instances. Accurate diagnosis in any tumor depends on tissue study and intrathoracic neoplasms are no exception. With the continued refinement of surgical and anesthetic techniques the procedure of exploratory thoracotomy has become an accepted one in all age groups. For this reason alone there seems to be little justification in overlooking the only certain method of diagnosis and treatment in the management of the solitary asymptomatic lung tumor.

#### SUMMARY

A series of twenty four case histories is presented. All of the patients were operated upon because of roentgen evidence of a solitary lung tumor.

The mortality rate was zero. One patient developed a partial hemothorax necessitating a partial decortication.

Four of the tumors proved to be malignant; seven were diagnosed as tuberculomas.

# CARCINOMA OF THE SUPERIOR MEDIASTINAL SEGMENT OF THE ESOPHAGUS

## A TECHNIQUE FOR RESECTION WITH RESTORATION OF CONTINUITY OF THE ALIMENTARY CANAL

RICHARD H. SWEET, M.D., BOSTON, MASS.

IT WAS suggested in 1949 that from the standpoint of surgical management of cases of carcinoma it is convenient to divide the thoracic portion of the esophagus into *fourths*. The upper fourth, or superior mediastinal segment, extends from the base of the neck to the superior margin of the aortic arch; the middle two fourths from the superior margin of the aortic arch to the level of the inferior pulmonary veins, and the lower fourth from that point to the diaphragm. At the time when this subdivision into segments was proposed, a satisfactory technique for the extirpation of carcinoma of the esophagus was available only in the case of a growth situated in the lower portion. This is the operation of partial esophagectomy and gastrectomy with a low intrathoracic esophagogastric anastomosis. For lesions in the middle half the Tork operation was still in use. In a short time, however, the operation of partial esophagectomy and primary esophagogastronomy was modified to include such cases and the Tork operation was abandoned.<sup>1, 2</sup>

For the removal of a lesion located in the upper fourth of the thoracic portion of the esophagus, on the other hand, no satisfactory technique has been developed up to the present time. A carcinoma in this segment is too low for the use of the Wokeley operation, which is applicable only in cases where the growth lies in the cervical region. It is too high for the performance of a supra-aortic intrathoracic esophagogastric anastomosis. It is unsuitable, furthermore, for the application of the Tork operation because of the fact that if the esophagus is divided high enough to avoid the upper margin of the tumor, the proximal portion is too short to make a satisfactory cervical esophagostomy. Recently a modification of the technique used for the removal of tumors in the midthoracic segment of the esophagus has been developed so that now a growth situated in the superior mediastinal segment can be resected and a primary esophagogastric anastomosis made in the neck using the short proximal esophageal stump.

### THE TECHNICAL PROBLEM

That the stomach can be mobilized sufficiently to make it possible to place the fundus in the apex of the left pleural cavity has been obvious for several years. This fact was discovered as a result of the adaptation of the operation of partial esophagectomy with primary intrathoracic esophagogastronomy to the removal of carcinoma high in the midthoracic region. In the case of carcinoma in the superior mediastinal segment of the esophagus it is impossible from within

benign only in the sense that it does not undergo neoplastic degeneration the benignity of the lesion ceases there.

It must also be pointed out that the age incidence of the patients presented in this series is comparatively young. Since these people were seen in a military hospital during wartime the reason is self-evident. A comparable series in which the average patient age exceeded 50 years would probably show a higher incidence of malignant tumors, thereby emphasizing even more the importance of surgical exploration in the presence of an asymptomatic lung tumor.

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A series of twenty four case histories is presented. All of the patients were operated upon because of roentgen evidence of a solitary lung tumor.

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ties and cut. These arise from the aortic arch, the bronchial arteries, and the descending aorta. In fixing the lower portion of the esophagus the posterior esophageal lymph nodes must be included in the dissection in so far as possible. After the entire thoracic portion of the esophagus has been dissected free the phrenic nerve is crushed and the diaphragm is incised from a point close to its costal insertion through the margin of the esophageal hiatus. This permits the mobilization of the stomach which is begun by dividing the attachments of the fundus, including the gastrosplenic ligament, the vascular axis, and the left gastroepiploic vessels. The entire gastrosplenic ligament is then incised all the way to the level of the pylorus, pains being taken to avoid injury to the anastomotic arcade of vessels along the greater curvature of the stomach through which a flow of blood is maintained by the right gastroepiploic artery. The left gastric vessels are tied and cut. The gastrohepatic ligament is incised as far as the level of the pylorus. Here likewise, the integrity of the venular arches along the lesser curvature which are supplied by the right gastric artery must be preserved. It is important to mention in this connection that the left gastric artery should be tied and cut close to its origin from the celiac axis to preserve its peripheral branches which furnish the greater portion of the vascular arcade along the lesser curvature.

After the mobilization of the stomach has been completed, the esophagus is cut across just above the cardia and the stump on the gastric side is inverted with a purse-string suture reinforced with a layer of Lembert sutures of silk. A piece of rubber tissue tied to the proximal end and the esophagus is then pulled up and out from behind the aortic arch so as to make its later withdrawal into the neck somewhat easier.

The completely mobilized stomach is then drawn up into the left thoracic cavity behind the hilum of the lung and lateral to the aortic arch. Fixation in this location is maintained by means of a series of interrupted silk sutures between the gastric wall and the mediastinal pleural surface which verifies the spreading of it. The fundus of the stomach is allowed to be free in the superior portion of the pleural cavity until the central portion of the operation is performed. The fixation sutures already applied prevent it falling down out of reach after the chest has been closed. The diaphragm is sutured to the stomach just above the pylorus and the remainder of the diaphragmatic incision is closed.

A Foley catheter is led out through a small incision in the tenth intercostal space posteriorly. To complete the first stage of the operation the lungs are spanned with anasthetist and the thoracotomy incision is closed using interrupted silk sutures in all layers.

(2) Second Stage of the Operation—*Perforation of the Intracranial Esophagus for Anastomosis*—After closure of the thoracotomy incision has been completed, the patient is turned on his back and an incision is made along the inferior margin of the left trapezius muscle to the supra-axillary notch and then downward vertically over the upper portion of the sternum to the level of the second costal cartilage. The posterior major muscle is incised close to its insertion and reflected laterally at the same time severing its insertion

the thoracic cavity to reach beyond the proximal border of the growth for division of the esophagus. A separate cervical incision must therefore be used for that purpose. The problem then arises as to how to bring the fundus of the previously mobilized stomach from the apex of the left pleural cavity into the neck where the esophagogastric anastomosis must be made.

The space through which the esophagus normally passes from the neck into the superior mediastinum is not large enough to accommodate the fundus of the stomach. Furthermore, even if the fundus could be forced through this narrow passageway between the trachea and the spine there would not be room enough to perform a satisfactory anastomosis in the space available between the spine, the trachea, and the carotid sheath. As a second alternative, the fundus might be brought out through a short anterior incision in the second intercostal space and then up into the neck through a subcutaneous tunnel. The obvious objection to this possibility is that the pressure of the overlying skin, fascia, and muscle would cause too much compression of the stomach and the anastomosis against the underlying structures. Ample room can be obtained, however, by resecting the inner one-half of the clavicle and a comparable segment of the first rib so that the fundus can be passed into the neck without pressure or constriction to meet the short high-lying proximal esophageal segment. This technique was developed to overcome the difficulty of restoring the continuity of the alimentary canal in a patient with congenital atresia of the esophagus who had been treated by closure of the tracheoesophageal fistula and the establishment of a cervical esophagostomy and a gastrostomy instead of by primary anastomosis. This case has been reported elsewhere.

# DESCRIPTION OF THE OPERATION

The operation is performed in one stage as follows:

(1) *First Step of the Procedure—Dissection of the Esophagus and Mobilization of the Stomach*—The patient is placed on the right side with the left arm held forward, the hand in front of the face. A long oblique incision is made along the course of the eighth rib from the costal margin in front to within a few centimeters of the midline in back, where it is made to curve upward between the spine and the scapula a short distance. The eighth rib is resected, cutting its neck posteriorly and the cartilage anteriorly. A rib spreader is inserted. If sufficient exposure is not available to reach the superior mediastinum, the seventh, sixth, and sometimes the fifth ribs may be divided posteriorly. The dissection is begun in the region of the tumor after opening the mediastinal pleura above the aortic arch behind the left subclavian artery. If the tumor-bearing portion of the esophagus can be freed sufficiently to make it possible to perform an anastomosis, the entire upper fourth is identified.

as it crosses the esophagus just above the aortic arch. If the wall is invaded by tumor or is too adherent to be dissected free, or if it has been injured during the dissection, it must be ligated to prevent the development of a chyloous hydrothorax after operation. Below the aortic arch the esophageal arteries must be





in the medial portion of the clavicle. The sternal and medial clavicular insertions of the sternocleidomastoid muscle are severed and retracted laterally. The dissection is then deepened in the space between the carotid sheath and the trachea to expose the esophagus. By grasping it with a forceps the esophagus is pulled up from the mediastinum and out in front of the carotid sheath.

The medial half of the clavicle and a corresponding segment of the left first rib and costal cartilage are resected extrapersonally. The clavicle should be cut with the high saw. This produces a large opening from the base of the neck behind the lower end of the sternomastoid muscle into the apex of the left pleural cavity through which the fundus of the stomach can be drawn easily and without danger of compression. The esophagus is pulled up from the mediastinum and out in front of the carotid sheath. The fundus is then brought forward medial to the apex of the lung and pulled up into the lower portion of the neck (Fig. 1). A short incision is made in the posterior wall of the fundus close to its apex and an anastomosis consisting of three layers of interrupted fine silk (00000) sutures is made. A careful approximation of mucosa to mucosa and muscle edge-to-muscle edge constitute the inner and middle layers. The outer layer is of mattress sutures. Several sutures are used to fix the fundus to the surrounding tissues of the neck to prevent tension on the anastomosis which, after its completion, lies in front of the carotid and internal jugular vessels (Fig. 2). The wound is closed by suturing the lower end of the sternocleidomastoid muscle and the medial cut edge of the pectoralis major muscle to the sternum and placing a layer of fine silk sutures in the subcutaneous fat and another in the skin. The wound is not drained.

#### CASE REPORT

As an illustration of the utilization of this operation in the management of carcinoma of the superior mediastinal segment of the esophagus, the following case report is submitted:

J. R., white man, aged 65 years, entered the Baker Memorial unit of the Massachusetts General Hospital on Oct. 22, 1947. About three months previously he had noticed certain amount of difficulty with swallowing when he choked on pieces of bread. This did not occur again for considerable period of time but a few weeks before admission he had begun to notice difficulty swallowing other foods, particularly bread. Following that time the dysphagia became increasingly noticeable so that he had to be very careful about what he ate although he was able to eat fairly liberal diet. He had not lost much weight or strength and was still able to carry on his work. He had never been ill in his life before this episode.

Rosengren ray examination of the throat showed lesions in the retrosternal region behind the manubrium of the sternum and he was therefore referred to the Baker Memorial for consideration of resection of the esophagus.

Physical examination revealed man apparently in an excellent state of health. Blood pressure was slightly elevated, 160/100 but the heart sounds were normal. No murmurs could be heard.

Laboratory studies revealed white blood count of 7,200 and hemoglobin of 15.4 Gm. per cent. There are 84 polymorphonuclear cells, 10 small lymphocytes and 2 monocytes. The stained specimen showed normal red blood cells and platelets with several polymorphonuclear cells showing toxic granules. The serum protein was 5.2 Gm. per cent. The

phragm. The diaphragm was then incised. There were no evidences of metastases within the abdomen but there was a lymph node along the lower portion of the esophagus just below the diaphragm which seemed to be invaded by the tumor. The liver was free from palpable nodules.

The stomach was not large but it was readily mobilized. A incision was made as performed during all of the cases except the right gastric and the right gastroepiploic arteries and veins and securing the gastrophrenic and gastrosplenic ligaments of possible to the right. A heavy tie of silk was placed around the esophagus just below the cardia and the esophagus was cut en masse with a knife. The proximal end was covered with a piece of rubber tubing tied on to the distal end. It was filled with silk suture string cut in two. This was used to feed with several interrupted Lembert sutures of fine silk. The esophagus was then pulled up from below and the anastomosis made.



FIG. 1.—A photograph of the specimen showing the primary tumor. The upper end of the esophagus is closed to contain the liquid. The lower end which is closed to contain the liquid.

The dissection was carried out as far as possible. The stomach was then pulled up and the esophagus was pulled from below and the anastomosis was made. The stomach was then pulled up and the esophagus was pulled from below and the anastomosis was made. The stomach was then pulled up and the esophagus was pulled from below and the anastomosis was made.

Asaprotein nitrogen 2. mg per cent and the chloride 102 mg per cent. The prothrombin time was 17 (normal 18) seconds, and the fasting blood sugar 117 mg per cent. Electrocardiogram showed no abnormality of the heart.

Röntgen ray examination of the upper gastrointestinal tract showed considerable enlargement of the upper esophagus. There was no retraction of the upper esophagus, leading to about 6 cm. opposite the third, fourth, and fifth dorsal vertebrae from approximately the level of the lower third midpoint of the aortic arch. There was no evidence of obstruction but the esophagus was somewhat narrowed in the region, irregular in appearance and showed definite destruction of the greater portion of its lumen with a definite shelf-like edge at the upper margin of the lesion (Fig. 3). The caudal side of the esophagus appeared normal. The stomach, duodenum and upper small intestine of the patient had no abnormality.

Röntgen ray examination of the chest showed the lungs to be clear with no demonstrable evidence of metastases, the pulmonary pathology. The heart was normal in shape and position. There was no evidence of pleural effusion or other abnormality.



FIG. 3. J. J. Murphy's center camera showing the filling defect produced by the polypoid mass in the superior mediastinal segment of the esophagus at the level of the constriction of the aortic arch.

After 8 days of preliminary preparation the patient was operated upon October 1947. A long oblique incision was made down the left side of the chest and the eighth rib was resected. A rib spreader was inserted and good exposure of the entire mediastinum was obtained. A retractor made of the second rib and pleura along the aortic arch and the esophagus was inserted. The trachea lay below the level of the aortic arch and the proximal vena cava passed up the base of the neck. There was considerable periesophageal adhesion with marked thickening which made the dissection difficult, especially between the esophagus and the trachea. During this dissection the thoracic duct was identified. A strand of heavy silk was passed around the thoracic duct to retract it. The duct was not injured in the course of the procedure and therefore it was not ligated.

When it became apparent that the growth could be dissected from the dissection was carried down behind the aortic arch and incision was made in the pleura below the arch all the way to the diaphragm. The esophagus was freed from the arch to the dia-

phragm. The diaphragm was then opened. There were no I seen f met v t nes with the abdomen, but there was lymph on long th two portions of the esophagus just below the diaphragm which seemed to be ded by tumor. The l er wa free from palpable nodules.

The stomach was a t large but t read l m l l e d l a sten m o d l i r t i o n was performed d m t g h f the m e d l t e p e t the u p t g e t e r and the u h e g a s t r o e p h a g e s t e r e s e d e s e d m o v e r i n g t h g e s t a l e p a t a n d g a s t r o e s o l i t a t e m e n t f a s p o s s i b l e t t h e r i g h t A h e a y t f a l k a p l a c e d r o u n d t h e e s o p h a g u s j u s t b e l o w t h e c a r d i a a n d t h e e s o p h a g u s c u t c r o s s w i t h h f T h p r o x i m a l e n d w a e r e d w i t h a p e e c e f r o b i l e t r a n s t e d t h d e t l l w e r e d w i t h a w i l k p a s s e s t r i n g e t c e T h e w e f r e e l w i t h a n e a l t e m p t e d L e m b e r t a n d r e s f f i n e d l k T h e e s o p h a g u s w t h e n p u l l e d p f r o m b e h a n d t h m o r t h

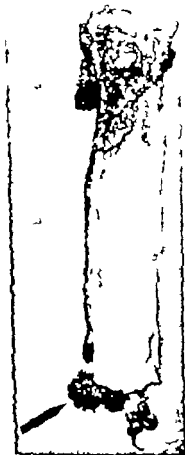


Fig. 1. — Photograph of the specimen after removal of the stomach and esophagus. The large, dark, irregular mass at the bottom is the tumor. The esophagus is visible above it.

The dissection was made of the stomach and esophagus. The stomach was opened and the contents were removed. The esophagus was then pulled out and the tumor was seen. The tumor was a large, dark, irregular mass at the bottom of the esophagus. It was surrounded by a layer of tissue. The tumor was removed and the esophagus was closed. The stomach was then closed and the patient was returned to the operating table.



Fig 5.—Case J. S. Postoper. h. fluorogram showing suprasternal loc. of the chest and base of the neck after the insertion of barriers. The fusion of the stomach and the anastomosis are seen lying above the level of the suprasternal notch.



of sutures between the mediastinal pleura overlying the descending aorta and the posterior gastric wall. The lung was then expanded and the chest wall was closed using interrupted silk sutures. A Foley catheter was brought out through one of the lower intercostal spaces. Streptomycin and penicillin solution injected both above and below the diaphragm.

The patient was then turned on the back and oblique incision was made along the course of the left sternocleidomastoid down as far as the jugular notch. This was then curved downward over the left half of the sternum to the level of the second costal cartilage. This incision was carried into the deep planes of the neck into the retropharyngeal sheath. The pretracheal muscles were separated from their origin from the sternum and the superior mediastinum was entered through the deep planes of the neck.

The esophagus was pulled out. There was actually about 3 to 4 cm length available for the anastomosis. It was not possible to pull the stomach up through the perithoracic thorax into the base of the neck and hence room enough to perform anastomosis. The attachment of the sternocleidomastoid muscle and of the pectoral muscle to the lower third of the clavicle were separated from the bone and the pectoralis major to the sternum was reflected latissimally along with the fat and skin as a single flap. The medial third of the clavicle was resected and the anterior half of the first rib. The proximal ends of the manubrium of the sternum which was 1 ft after disarticulating the first rib and the clavicle was cut with bone cutters. This removal of portions of bone made large round passages down to the pleura.

The pleura of the perithoracic left pleural sac was then closed and the fundus of the stomach was grasped and pulled out through the wound. It was brought up to the neck without much difficulty and an esophagojejunostomy was performed on the posterior aspect of the fundus using three layers of interrupted silk sutures. Instead of excising a circular portion of the gastric wall, simple linear incision was used. Because of series of sutures to adjust the fascial structure the fundus was supported, the base of the neck and the lower third of the sternocleidomastoid and pectoral muscles were sutured on its front to the sternum and to the adjacent fascia. The fat and skin were then closed as separate layers using silk throughout. No drainage was used, the cervical wound.

The report of the pathologist after examination of the specimen revealed the tumor to be squamous cell carcinoma, grade 3 with metastasis to one regional lymph node.

The patient withstood the operation very well and made good postoperative recovery. During the first four days of the postoperative course particularly when he was turned on the left side the pulse rate suddenly became very rapid at times and he had marked fall in blood pressure. Both of these signs disappeared when he was turned the back again. It is believed that this is due possibly to stimulation of the carotid sinus. The diet was allowed somewhat more slowly than the average case of resection of the esophagus but with timely discharge from the hospital fourteen days after operation, the swallowing function as normal and he was taking diet of small hopped feed. Subsequent reports reflect that he has continued to improve. He eats normally and has gained weight and strength.

#### COMMENT

The operation described offers an acceptable method of treatment of carcinoma located in the superior mediastinal segment of the esophagus where resection with restoration of continuity of the alimentary canal has hitherto been impossible. It obviates the necessity of either a gastrostomy or a cervical esophageal stoma. The patient is enabled to swallow normally and to eat a normal diet. The functional result is good.

From the standpoint of long time survival it is obvious that only the accumulation of experience with the use of this procedure in a group of patients

will prove its value. It should be pointed out, however, that unless the growth is early and small without evidence of local invasion of surrounding structures, the probability of local recurrence is great because of the fact that the dissection must of necessity be carried out close to the diseased area. This unavoidable fault is characteristic of all resections of the esophagus with the exception of those cases in which the growth lies near the cardia, but in the neck and superior mediastinum the narrowness of the operative field makes the difficulty even greater.

This fact, however, should not be allowed to militate against the decision to resect these tumors if it is at all possible to remove them. The pitiable plight of a patient with carcinoma of the esophagus who must die without the benefit of a resection should urge the surgeon on.

To cure such a patient is a blessing to be hoped for but probably not to be obtained in a large number of cases. To provide relief from dysphagia and to insure the comforts of normal eating are the greatest benefits which can be expected in the majority of cases. Those who are familiar with the end stages of this disease in the untreated patient will agree that this alone makes the operation worthwhile.

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# STUDIES ON ONE HUNDRED FIFTY-ONE PATIENTS AT THE UNIVERSITY HOSPITAL IN RELATION TO THEIR DAILY WEIGHT FLUCTUATIONS

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THE following is a study made on all adult patients at the University Hospital at Minneapolis who had surgery performed on the stomach and intestines during the first six months of 1940. This group of patients was chosen because all of them were under the supervision of the same members of the surgical staff and also because all of them were weighed daily during their stay in the hospital.

Each patient in this group was weighed in so far as was possible each morning after evacuation of the bladder and before they had been given their breakfast. All of those who were able to do so stood on the scale which was brought to the bedside but for those patients who were unable to get out of bed a special scale was ingeniously contrived which it was possible to weigh them in bed.

Concurrently with the weight study with the daily weight fluctuations, a record was kept of the total nasogastric fluid intakes and output of each patient both quantitatively and qualitatively.

During the same six-month period there were a total of 1,340 operations performed at the University Hospital in the Surgical Series and this group of major operations performed on the stomach and intestines numbered 11 or 1.1 per cent of the total.

All patients in this group were of the white race with the average age was 58.9 years. The sex distribution was as follows: ninety-seven or 64 per cent were males and fifty-four or 35 per cent were females. There were fourteen deaths, or 9.4 per cent mortality in this series of patients.

The primary pathological condition in these patients was as shown in Table I.

The type of operative procedure performed on these patients was as shown in Table II.

In the surgical procedures listed in Table II it is to be noted that only the primary surgical procedure included the esophageal procedure (for example the gastroyjunostomy performed at the time of a gastric resection) and additional procedures (if any) performed at the same time were omitted.

A minimum of physical examination of each patient was made in the morning before being given any fluids either orally or parenterally. These weights are a measure of the physical condition of the patients preceding



will justify its value. It should be pointed out, however, that unless the growth is small and small without violence of local invasion of surrounding structures, the probability of local recurrence is great because of the fact that the dissection must of necessity be carried out close to the diseased area. This unavoidable fault is characteristic of all excisions of the esophagus with the exception of those cases in which the growth lies near the cardia but in the neck and superior mediastinum the narrowness of the operative field makes the difficulty even greater.

This fact, however, should not be allowed to militate against the decision to resect these tumors if it is at all possible to remove them. The pitiable plight of a patient with carcinoma of the esophagus who must die without the benefit of a resection should urge the surgeon on.

To cure such a patient is a blessing to be hoped for but probably not to be obtained in a large number of cases. To provide relief from dysphagia and to insure the comfort of normal eating are the greatest benefits which can be expected in the majority of cases. Those who are familiar with the end stages of this disease in the untreated patient will agree that this alone makes the operation worthwhile.

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# STUDIES ON ONE HUNDRED FIFTY ONE PATIENTS AT THE UNIVERSITY HOSPITAL IN RELATION TO THEIR DAILY WEIGHT FLUCTUATIONS

ALBERT DULIVAN, JR. M.D. MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

THE following is a study made on all adult patients of the University Hospital at Minneapolis who had surgery performed on the stomach, colon, or rectum during the first six months of 1946. This group of patients was chosen because all of them were under the supervision of the same members of the surgical staff and also because all of them were weighed daily during their stay in the hospital.

Each patient in this group was weighed in so far as was possible each morning after evacuation of the bladder and bowel and before they had been given their breakfast. All of these who were able to do so stood on the scale which was brought to the bedside but for those patients who were unable to get out of bed a special scale was employed in the room of which it was possible to weigh them in bed.

Concurrently with the record kept of their daily weight fluctuations, a record was kept of the total measurable fluid intakes and outputs of each patient both quantitatively and qualitatively.

During this same six month period fifteen major abdominal operations were performed at the University Hospital in the surgical service and this group having surgery performed on the stomach, colon, or rectum numbered 111 or 74 per cent of the total.

All patients in this group were of the white race and their average age was 59 years. The sex distribution was as follows: ninety seven or 64 per cent were males and thirty four or 28 per cent were females. There were fourteen deaths or a 9.4 per cent mortality in this series of patients.

The primary pathological condition in these patients was as shown in Table I.

The type of operative procedure performed on these patients was as shown in Table II.

In the surgical procedures listed in Table II it is to be noted that only the primary surgical procedure is included. In all laparotomy procedures (for example the gastrojejunostomy performed at the time of a gastric resection) and all nonoperative procedures (for example in left appendectomy) are omitted.

An informed physician who has patients weighed in the morning before breakfast and fluids with them will find that all of these weight measurements with the patient in bed are still in good agreement with the preceding

will prove its value. It should be pointed out, however, that unless the growth is early and small without evidence of local invasion of surrounding structures, the probability of local recurrence is great because of the fact that the dissection must of necessity be done in close to the diseased area. This unavoidable fault is characteristic of all resections of the esophagus with the exception of those cases in which the growth lies near the cardia, but in the neck and superior mediastinum the narrowness of the operative field makes the difficulty even greater.

This fact, however, should not be allowed to militate against the decision to resect these tumors if it is at all possible to remove them. The pitiable plight of a patient with carcinoma of the esophagus who must die without the benefit of a resection should urge the surgeon on.

To cure such a patient is a blessing to be hoped for but probably not to be obtained in a large number of cases. To provide relief from dysphagia and to insure the comfort of normal eating are the greatest benefits which can be expected in the majority of cases. Those who are familiar with the end stages of this disease in the untreated patient will agree that this alone makes the operation worth while.

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# STUDIES ON ONE HUNDRED FIFTY-ONE PATIENTS AT THE UNIVERSITY HOSPITAL IN RELATION TO THEIR DAILY WEIGHT FLUCTUATIONS

ALBERT SULLIVAN, JR., M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

THE following study was made on all adult patients at the University Hospital at Minneapolis who had surgery performed on the stomach, colon, or rectum during the first six months of 1940. This group of patients was chosen because all of them were under the supervision of the same numbers of the surgical staff and also because all of them were weighed daily during their stay in the hospital.

Each patient in this group was weighed in so far as was possible each morning after evacuation of the bladder and bowel and before they had been given their breakfast. All of those who were able to do so stood on the scale which was brought to the bedside but for those patients who were unable to get out of bed a special scale was employed in lieu of which it was possible to weigh them in bed.

Concurrently with the record kept on their daily weight fluctuations, a record was kept of their total measurable fluid intakes and output of each patient both quantitatively and qualitatively.

During the same six-month period the same was a total of 1,240 operations performed at the University Hospital in the Surgery Service and this group having surgery performed on the stomach, colon, or rectum numbered 11.7 per cent of the total.

All patients in this group were of the white race and their average age was 58.9 years. The sex distribution was as follows: ninety-seven, or 64 per cent, were males; fifty-four, or 4.8 per cent, were females. There were fourteen lacerations, or 9.4 per cent mortality in this series of patients.

The primary pathological condition in these patients was as shown in Table I.

The type of operative procedure performed on these patients was as shown in Table II.

In the surgical procedures listed in Table II it is to be noted that only the primary surgical procedure is included and the accompanying procedures (for example, the gastrectomy performed with the total gastrectomy resection) and the procedure of removal of the appendix are omitted.

A mention of the procedure of weighing patients was made in the preceding paper in which it was stated that the patient was weighed in the morning before breakfast and the fluid intake and output were recorded. The weight was measured by the physician in the morning before the procedure.

Received for publication, February 1, 1941.

will prove its value. It should be pointed out, however, that unless the growth is early and small without evidence of local invasion of surrounding structures, the probability of local recurrence is great because of the fact that the dissection must of necessity be carried out close to the diseased area. This unavoidable fault is characteristic of all resections of the esophagus with the exception of those cases in which the growth lies near the cardia, but in the neck and superior mediastinum the narrowness of the operative field makes the difficulty even greater.

The fact, however, should not be allowed to militate against the decision to resect these tumors if it is at all possible to remove them. The pitiable plight of a patient with carcinoma of the esophagus who must die without the benefit of a resection should urge the surgeon on.

To rescue such a patient is a blessing to be hoped for but probably not to be obtained in a large number of cases. To provide relief from dysphagia and to insure the comforts of normal eating are the greatest benefit which can be expected in the majority of cases. Those who are familiar with the end stages of this disease in the untreated patient will agree that this alone makes the operation worth while.

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# STUDIES ON ONE HUNDRED FIFTY-ONE PATIENTS AT THE UNIVERSITY HOSPITAL IN RELATION TO THEIR DAILY WEIGHT FLUCTUATIONS

ALBERT SULLIVAN JR. M.D. MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

THE following study was made on all adult patients at the University Hospital at Minneapolis who had surgery performed on the stomach, colon, or rectum during the first six months of 1940. This group of patients was chosen because all of them were under the supervision of the same members of the surgical staff and also because all of them were weighed daily during their stay in the hospital.

Each patient in this group was weighed in so far as was possible each morning after evacuation of the bowels and before they had been given their breakfast. All of these were weighed on the same scale which was brought to the bedside but for those patients who were unable to get out of bed a special scale was employed by means of which it was possible to weigh them in bed.

Concurrently with the recording of the daily weight fluctuations, a record was kept of the total measurable fluid intake and output of each patient both quantitatively and qualitatively.

During this same six month period of time there was a total of 1,240 operations performed at the University Hospital in the Surgical Service and this group having surgery performed on the stomach, colon, or rectum numbered 111 or 9 percent of the total.

All patients in this group were of the white race and the average age was 59 years. The sex distribution was as follows: 64 percent were males and 36 percent were females. There were fourteen deaths or a 9.4 percent mortality in this series of patients.

The primary pathological condition in these patients has been shown in Table I.

The type of operation performed on these patients was as shown in Table II.

In the surgical procedures listed in Table II it is to be noted that in the primary surgical procedure included in such a group of procedures (for example the gastrectomy procedure) the two stages of the procedure (the initial procedure and the final procedure) are listed separately in parentheses.

As mentioned previously, each patient was weighed in the morning before breakfast and any fluid intake or output during these weight measurements of the physiologic studies of the patient were recorded.

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TABLE I

DIAGNOSIS	TOTAL	PER CENT
Gastric resection	23	21.8
Ileocecal ulcer	34	21.2
Rectal denudation ome	22	14.6
Colonic carcinomas	19	12.8
Gastric ulcer	18	10.4
Ulcerative colitis	8	12
Gastric lymphosarcoma	4	3.6
Esophageal carcinoma	4	6
Rectal polypoids	3	0
Malfunctioning colon	3	2.8
Colonic polypoids	3	1.3
T hernia ulcer of colon	2	1.3
Rectovaginal fistula	1	0.7
I inflammatory colonic stricture	1	0.7
Ovarian carcinoma (spread)	1	0.7
Chronic proctitis	1	0.7
Rectal lymphosarcoma	1	0.7
Colonic diverticula	1	0
Total	151	100.0

TABLE II

Abdomino-perineal resection	8	6
Total gastrectomy	6	4.0
Total colectomy	3	3.3
Gastrojejunostomy	5	3.3
Gastrectomy	4	2.6
Colostomy closure	4	6
Exploratory laparotomy	3	2
Pull-through operation	2	1.3
Gastrectomy	3	1.3
Proctectomy	2	0.7
Proctotomy	1	0.7
Closure perforated duodenal ulcer	1	0.7
Total	151	100.0

TABLE III

POSTOPERATIVE DAY OF WEIGHT LOSS	NUMBER	PER CENT OF TOTAL
1st	14	4.4
2nd	4	32.4
3rd	10	12.8
4th	13	8.6
5th	10	6.6
6th		1.3
7th	3	2.0
8th and after	6	4.0
Loss of less than 1/4% total body weight	44	19.8
Not recorded preoperatively	1	4.0
Total	151	100.0

With this view in mind, it was noted that 116 of these patients, or 68 per cent, showed weight losses of as much as  $9\frac{1}{2}$  per cent of their total body weight following surgery. The day on which this loss occurred is listed in Table III.

The average amount lost by those patients who had a weight loss of as much as  $\frac{1}{2}$  per cent of their total body weight was 3 kg. However when computed on a percentage basis we have the findings shown in Table IV.

TABLE IV

PER CENT OF TOTAL BODY WEIGHT LOST	NUMBER	PER CENT OF TOTAL
Less than $\frac{1}{2}$	24	18.6
$2\frac{1}{2}$	37	4.6
3	14	11.9
$3\frac{1}{2}$	16	10.1
4	1	11.2
4	6	2.9
6	16	10.6
6	6	1.9
Greater than 6	7	0
Not recorded properly	7	4.6
Total	151	100

In an attempt to determine the cause of these losses in body weight the average intake for the day preceding the weight loss (see above) was determined and was found to be 3,290 cc. The total output for this same day averaged 5,535 cc of which 40 per cent was urine and 9 per cent was from gastric secretion, and 19 per cent was from other sources, such as emesis, bile, thoracentesis.

Since the greatest loss of fluid was from urine it was thus considered necessary to determine those factors which might stimulate urinary output or which might cause retention of body water. To this end it was found that of the total fluid intake on the day preceding the weight loss, 31.3 per cent was 10 per cent glucose solution and this was given along with an average of 6.0 gm of sodium chloride. Thus, it seems that we have here an inhibitor against both the 10 per cent glucose and also against the small amount of sodium chloride given. In the case of the 10 per cent glucose it cannot be stated that the blame must rest upon it per se because it must be taken into account that rapid administration of this solution is quite effective in causing diuresis.

In an attempt to determine what effect it might be playing in those patients who did not have a weight loss, or whose weight loss exceeded 4 per cent, separate analyses were made of these two groups which comprised 185 and 203 per cent, respectively of the total group of patients. For purposes of tabulation, the three groups are listed as follows in Tables V and VI.

- Complete series of 151 patients
- Those patients whose weight loss was not as much as  $9\frac{1}{2}$  per cent who showed an actual gain in weight
- Those patients whose weight loss exceeded 4 per cent of their total body weight.



TABLE I

DEADLY DISEASE	TOTAL	PER CENT
Gastric carcinoma	33	31.8
Duodenal ulcer	22	21.2
Rectal adenocarcinoma	22	14.6
Colonic carcinoma	19	12.6
Gastric ulcer	18	10.6
Ulcerative colitis	5	3.3
Gastric lymphosarcoma	4	2.6
Esophageal carcinoma	4	6
Rectal polypoid	3	8
Malignant ulcer of colon	3	2
Colon polypoid	3	1.3
Tuberculous ulcer of colon	2	1.3
Rectovaginal fistula	1	0.7
Inflammatory colonic stricture	1	0.7
Ovarian cancer omentum spread	1	0.7
Chronic proctitis	1	0.7
Rectal lymphosarcoma	1	0.7
Colonic diverticula	1	0
<b>Total</b>	<b>181</b>	<b>100%</b>

TABLE II

OPERATION	NUMBER	PER CENT OF TOTAL
Partial gastrectomy	66	36.5
Partial colectomy	44	24.3
Colectomy or ileostomy	15	8.3
Abdominal peritoneal resection	8	4.4
Total gastrectomy	6	3.3
Total colectomy	5	2.7
Gastrojejunostomy	0	0
Gastrectomy	4	2.2
Colectomy ileostomy	4	2.2
Exploratory laparotomy	3	1.6
Full-thickness operation	3	1.6
Gastrectomy	3	1.6
Proctectomy	1	0.5
Proctostomy	1	0.5
Closure perforated colon & liver	1	0.5
<b>Total</b>	<b>181</b>	<b>100%</b>

TABLE III

POSTOPERATIVE OF WOUND LOSS	CASES	PER CENT OF TOTAL
1st	12	6.6
2nd	19	10.5
3rd	14	7.7
4th	15	8.3
5th	10	5.5
6th	5	2.7
7th	3	1.6
8th and after	6	3.3
Loss of less than 3 1/4% total body weight	74	40.9
Not recorded properly	7	3.9
<b>Total</b>	<b>181</b>	<b>100%</b>

With this view in mind it was noted that 116 of these patients, or 76.8 per cent showed weight losses of as much as 93 per cent of their total body weight following surgery. The day on which this loss occurred is listed in Table III.

The average amount lost by those patients who had a weight loss of as much as  $\frac{1}{2}$  per cent of their total body weight was 9.3 kg. However when computed on a percentage basis we have the findings shown in Table IV.

TABLE IV

PER CENT OF TOTAL BODY WEIGHT LOST	NUMBER	PER CENT OF TOTAL
Less than $\frac{1}{8}$	44	14.8
$\frac{1}{8}$	37	4.6
$\frac{1}{4}$	18	11.9
$\frac{3}{8}$	13	10.1
$\frac{1}{2}$	17	11.2
$\frac{3}{4}$	6	3.9
5	16	10.6
6	6	3.9
Greater than 6	1	0.7
Not recorded properly	7	4.6
Total	151	100.0

In an attempt to determine the cause of these losses in body weight the average intake for the day preceding the weight loss (see above) was determined and was found to be 3,299 cc. The total output for this same day averaged 3,000 cc of which 0.5 per cent was urine, 27.6 per cent was from gastro suction, and 19 per cent was from other sources, such as emesis, bile thoracentesis, etc.

Since the greatest loss of fluid was from urine it was thus considered necessary to determine those factors which might stimulate urinary output or which might cause retention of body water. To this end it was found that of the total fluid intake on the day preceding the weight loss, 51.3 per cent was 10 per cent glucose solution and this was given along with an average of 6.5 Gm of sodium chloride. Thus, it seems that we here have an indifferent against both the 10 per cent glucose and also against the small amount of sodium chloride given. In the case of the 10 per cent glucose it cannot be stated that the blame must rest upon it per se because it must be taken into account that rapid administration of this solution is quite efficacious in causing diuresis.

In an attempt to determine what factors might be at play in those patients who did not have a weight loss, or whose weight loss exceeded 4 per cent, separate analyses were made of these two groups which comprised 185 and 303 per cent, respectively of the total group of patients. For purposes of tabulation, the three groups are listed as follows: Tables V and VI.

- Complete series of 11 patients
- Those patients whose weight loss was not much as  $\frac{1}{2}$  per cent or who showed an actual gain in weight
- Those patients whose weight loss exceeded 4 per cent of their total body weight.

TABLE V

		B		
Average age		59.0 yr	56.3 yr	58.1 yr
Sex		61.2%	53.0%	65.1%
Males				
Females		31.9%	46.4%	31.9%
Average intake		1200	1233	1178 c.
Per cent of intake	high	10% glucose	51.3%	56.0%
Average output		1313	1373	1025
Per cent of output	high as urine	70.8%	5.8%	64.3%

TABLE VI

OPERATION	NO.	PER CENT	PER CENT	NO.	PER CENT	
Total gastrectomy	66	43.6	14	46.5	31	41.7
Partial colectomy	4	1.6	6	1.3	1	2.7
Colonostomy	13	9.9	2	7.1	1	3.1
Abdominoperitoneal resection	8	5.4	1	3.6	2	4.9
Total gastrectomy	6	4.0	3	10.8	4	8.6
Total colectomy	5	3.3	0	0.0	1	3.1
Gastrojejunostomy	5	3.3	1	3.6	1	3.1
Gastrostomy	4		0	0.0	1	3.1
Colostomy (low)	4	6	0	0.0	1	3.1
Exploratory laparotomy	3	2.0	2	7.1	1	3.1
Pull through operation		1.3	0	0.0	0	0.0
Gastrostomy	2	1.3	0	0.0	0	0.0
Proctectomy	1	0.7	0	0.0	1	3.1
Proctostomy	1		0	0.0	0	0.0
Closure perforated duodenal ulcer	1	0.7	0	0.0	0	0.0
Totals	151	100.0	54	100.0	48	100.0

Statistically analyzed non of the minor variations noted here among the three groups is significant with all three showing the same general trends and tendencies, except for the fact that in those patients who did not lose as much as  $\frac{1}{2}$  per cent of their total body weight there was a marked diminution in total fluid output, and in those patients showing a weight loss of as much as or more than 4 per cent there was a slight increase in the average fluid output.

## CONCLUSIONS

A study was made on all adult patients having surgery performed on the stomach, colon or rectum during the first six months of 1946 in relation to their daily weight fluctuations. This group of patients comprised 1.1 per cent of all patients undergoing surgery in the main operating rooms at the University Hospitals during the same period of time (Orthopedic, gynecologic and otolaryngologic surgery is performed in their own operating rooms). There were fourteen deaths or a 9.4 per cent mortality in this series of patients.

One hundred sixteen, or 76.8 per cent, of these patients showed a weight loss of as much as  $2\frac{1}{2}$  per cent of their body weight in the immediate postoperative period. Eleven, or 7 per cent of these patients, showed weight gains of .5 per cent or more of their body weight, and seventeen, or 11 per cent of the patients, showed no weight loss, gains of as much as  $2\frac{1}{2}$  per cent of their body weight, and their weight fluctuations bore no relation to a given operative procedure.

The day on which the largest percentage of patients lost weight was the second post operative day. Since the weights are taken each morning however this indicates that the greatest loss was on the first day following surgery.

The average weight loss per patient was 1 kg. The average fluid output on the day of weight loss was 4500 cc of which 90 per cent was urine.

The average fluid intake on the day of weight loss was 7200 cc of which 31.7 per cent was 10 per cent glucose, 1 per cent was 5 per cent glucose, 1 per cent was normal saline solution, 1 per cent was water (per os), 1.8 per cent was 5 per cent amylum, and the rest was hospital diet II.

Separate analyses of those groups of patients who showed no significant weight loss and of those whose weight loss exceeded 4 per cent of their total body weight revealed no significant factors in these groups which might make them differ from the original group except for the fact that the average output on those patients who had no significant loss of weight was approximately one half that of the average output of the whole group and that the average output on those patients showing weight loss greater than 4 per cent of their total body weight was approximately 50 per cent greater than that of the average output of the whole group.

TABLE V

			0
Average age	54.9 yr	54.3 yr	54.1 yr
Sex: Males	84.4%	83.6%	83.1%
Females	15.6%	16.4%	16.9%
Average intake	1,900	2,233	2,178
Per cent of intake which as 10% glucose	51.3%	51.3%	50.9%
Average output	2,333 cc	1,873	2,023
Per cent of output back urine	70.6%	73.8%	69.3%

TABLE VI

OPERATION	NO.	PER CENT	NO.	PER CENT
Total gastrectomy	41	11	41	41
Partial gastrectomy	196	6	217	13
Colostomy	99	2	1	21
Abdominoperineal resection	54	1	26	43
Total gastrectomy	40	3	109	4
Total colostomy	33	0	00	1
Gastrojejunostomy	33	1	36	1
Gastrostomy	6	0	00	1
Colostomy closure	26	0	00	1
Exploratory laparotomy	0	2	7.1	1
Pull through operation	13	0	00	0
Gastrostomy	13	0	00	0
Ileostomy	07	0	00	1
Proctostomy	7	0	00	0
Closure perforated duodenal ulcer	0	0	00	0
Totals	131	21	100	48

Statistically analyzed none of the minor variations noted here among the three groups is significant with all three showing the same general trend and tendencies, except for the fact that in those patients who did not lose as much as 1 per cent of their total body weight there was a marked diminution in total fluid output and in those patients showing a weight loss of as much as or more than 4 per cent there was a slight increase in the average fluid output.

## CONCLUSIONS

A study was made on all adult patients having surgery performed on the stomach, colon, or rectum during the first six months of 1946 in relation to their daily weight fluctuations. This group of patients comprised 1.1 per cent of all patients undergoing surgery in the main operating rooms at the University Hospital during the same period of time (Orthopedic, gynecologic and urologic surgery are performed in their own operating rooms). There were fourteen deaths, or a 9.4 per cent mortality in this series of patients.

One hundred sixteen, or 76.8 per cent, of these patients showed a weight loss of as much as 1.2 per cent of their body weight in the immediate post-operative period. Eleven, or 3 per cent of these patients, showed weight gains of 5 per cent or more of their body weight and nineteen, or 11 per cent of the patients, showed no weight loss or gain of as much as 1.2 per cent of their body weight. These weight fluctuations bore no relation to any operative procedure.

diameter with walls  $\frac{1}{64}$  inch thick) was inserted for a distance of 4 or 5 inches through a small hole made in the vein proximal to the clamp. The clamp was then removed and after replacing the vein, the incision was sutured, a length of tubing extending out through the skin. In some cases the vein was tied off distal to the point of tube insertion and sutures were also tied around the vein containing the plastic. A protective tight fitting rubber tubing previously adjusted, covered the length of plastic tubing which extended out from the vein. To secure the assembly sutures were passed through the skin and tied to a wire loop at the end of this rubber tubing which touched the skin and the tubing was then fixed to the neck or shoulder with collodion soaked gauze.

The subcutaneous needle or the needle inserted into the open end of the plastic tubing, was connected by rubber tubing to a graduated container suspended about six feet above the animal. Solution delivery was accomplished by gravity and the rate was controlled by a screw clamp and calibrated drop counting apparatus. In some experiments instead of gravity drip we employed very satisfactorily a fluid pump described by Bratton. Saline solution alone was given to intravenous dogs for one day following preparation to permit recovery from the sodium pentobarbital.

Sterile solutions of histamine dihydrochloride in 0.9 per cent NaCl were injected at rates of from 240 to 960 c.c. per twenty four hours, the smaller volumes being given by the subcutaneous method.

All but the first few dogs were given a vermifuge several days before starting the experiment to remove the complicating factor of intestinal worms which may cause or predispose to ulceration.

Drug administration was continuous, in so far as was possible, from the beginning of the experiment until death or until the animals were sacrificed usually after twenty-one days.

## RESULTS

*Subcutaneous Injection*—Histamine dihydrochloride was injected continuously into eighteen dogs, the daily doses ranging from 36 to 7 mg. of histamine base. Five animals were sacrificed after fourteen to twenty-one days, the remainder of the animals died during the course of the experiment. At autopsy after injection periods of from forty-one hours to twenty-one days, ulcers were found in twelve of these dogs, ulcer perforation occurring in seven animals. Erosions or duodenitis, or both, were observed in the dogs with ulcers and in five of the six animals which did not develop ulcers. Varying degrees of colitis appeared in some of the animals. One dog exhibited no apparent lesions.

Ulceration were frequently multiple and varied in size from acute lesions less than 0.5 cm. in diameter to deep craters 1.5 to 2 cm. across, the greater dimension usually being along the longitudinal axis. The larger ulcers had flat hard bases and raised indurated edges, the craters were sometimes filled with debris or blood clot. Ulcers regularly developed on the posterior wall of the duodenum within 0.5 to 3 cm. of the pyloric sphincter and often a kissing ulcer was found on the opposing portion of the anterior wall. In one case a

Smith, Rorhe, the histamine used in these studies as supplied by the Hoffman-La Roche, Inc., New York, N. Y.  
All dose values are in terms of histamine base.

PRODUCTION OF GASTRODUODENAL ULCERS IN THE DOG  
BY CONTINUOUS SUBCUTANEOUS OR INTRAVENOUS  
ADMINISTRATION OF HISTAMINE

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CONTINUOUS excessive secretion of highly acid gastric juice is considered to be an important factor in the pathogenesis of peptic ulcer. Since histamine strongly stimulates the secretion of HCl by the parietal cell, investigators have used this substance in attempts to produce ulceration of the gastrointestinal tract experimentally in animals. There are reports of erosions or ulcers found in guinea pigs, cats and dogs after injections one or more times daily for varying period of time, but workers in this laboratory were unable to obtain ulcers in dogs, although erosions were observed even when 1 mg. of histamine dihydrochloride were injected every two hours, ten times a day for over two months.

Intramuscular injections of a histamine and beeswax mixture as prepared by Code and Varco, in amounts of 30 to 40 mg. of histamine base daily have been shown regularly to produce ulcers in dogs and with appropriate doses in a variety of other animals. The histamine-beeswax preparation provides for a slow release of the drug and a sustained stimulation of gastric secretion throughout the twenty-four hour period. It appears from these results that a continuous histamine action is necessary for the production of experimental ulcer in the dog and that periodic subcutaneous injections of aqueous histamine solutions, even at two-hour intervals, do not satisfactorily produce such an action.

In the experiments to be described we have injected histamine continuously into a group of dogs by the subcutaneous route to determine whether ulcers would occur when the drug was so administered. In another group of dogs we have injected histamine continuously intravenously to test, by comparison of results obtained with the two methods, the possibility that an ulcerogenic agent is released from the tissues in the course of the local reaction to histamine or beeswax. Although Varco and associates have shown that beeswax injection alone will not cause ulceration, it is conceivable that two factors—histamine and some ulcerogenic agent released from the tissues—together might be responsible for the histamine ulcer.

We hoped from these experiments to find what dose-time relationships exist with respect to ulcer production in the dog and especially what minimal amount of histamine will cause ulceration within a limited period of time.

*Procedure*—Dogs weighing from 5 to 14 kilograms were given the continuous subcutaneous injections of histamine through a 3 inch long, 21 gauge needle inserted into the back and secured with straps. The position of the needle was changed every twelve hours, and the injection sites were shaved and washed with iodine and alcohol before inserting the needle.

Dogs which were to receive intravenous injection were anesthetized with sodium pentobarbital and an area at the base of the neck overlying an external jugular vein was prepared for surgery. The vein was exteriorized through a longitudinal incision and was clamped. A flexible, plastic tubing (3/64 inch inside

Subcutaneous inflammation was found at injection sites in the majority of the animals and was not prevented in four dogs when 100 units of penicillin per cubic centimeter was added to the solution being injected.

**Intravenous Injection.**—Histamine was administered intravenously and continuously in sixteen dogs, in doses of from 36 to 6 mg of base per day. Seven animals were sacrificed; the remainder died during the course of the experiment. Thirteen animals developed ulcers within sixteen hours or less, and perforation occurred in three dogs. Of the three dogs without ulcers, one had gastric and duodenal erosions, another duodenitis, and the third exhibited no lesions.

The distribution and the type of ulcer resulting from intravenous histamine injection were similar to that following subcutaneous histamine. The ulcers usually developed on the posterior wall of the duodenum within 1 to 3 cm below the pyloric sphincter and a healing ulcer was found on the anterior wall in four dogs. In three dogs ulcers appeared at the pyloric juncture. Ulceration occurred in the stomachs of two dogs. One had a small lesion 0.5 cm above the pyloric sphincter while the other had four ulcers at a distance of 6 cm above the pyloric sphincter, two of which ulcers had perforated. This latter finding is of interest and significance. The position of these four ulcers corresponded exactly to the openings in a Rehfuess tube olive which had been put in the dog's stomach for aspiration of gastric juice during an acute experiment performed the day before beginning continuous histamine injection. These ulcerations clearly indicate that the effect of mucosal injury is a plausible role in the production of experimental ulcers.

A conclusion that a minimal adequate dose of intravenous histamine is not warranted can be seen by reference to Table II. The latter suggests that doses

TABLE II. Effect of Histamine on the Development of Ulcers in Dogs

Dog	No. of Dogs	No. of Ulcers		No. of Dogs	No. of Ulcers	No. of Dogs	No. of Ulcers
		Stomach	Duodenum				
1	6	3	3	1	1	Sacrificed	Ulcers of duodenum 1 cm from pylorus
2	4	3	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
3	3	1	2	4	4	Died	Ulcers of duodenum 1 cm from pylorus
4	11	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
5	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
6	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
7	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
8	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
9	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
10	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
11	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
12	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
13	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
14	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
15	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
16	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
17	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
18	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
19	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
20	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
21	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
22	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
23	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
24	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
25	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
26	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
27	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
28	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
29	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
30	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
31	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
32	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
33	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
34	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
35	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
36	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
37	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
38	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
39	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
40	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
41	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
42	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
43	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
44	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
45	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
46	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
47	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
48	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
49	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
50	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
51	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
52	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
53	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
54	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
55	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
56	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
57	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
58	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
59	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
60	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
61	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
62	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
63	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
64	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
65	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
66	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
67	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
68	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
69	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
70	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
71	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
72	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
73	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
74	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
75	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
76	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
77	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
78	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
79	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
80	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
81	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
82	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
83	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
84	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
85	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
86	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
87	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
88	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
89	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
90	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
91	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
92	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
93	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
94	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
95	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
96	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
97	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
98	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
99	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus
100	1	1	1	1	1	Died	Ulcers of duodenum 1 cm from pylorus

Dogs were free of histamine ulcers when removed to the care of their dogs.



single ulcer occurred on the anterior wall of the duodenum. Ulcers were found at the pyloric sphincter in two dogs and in the pars intermedia of one dog. Two dogs had esophageal ulcers, one of which had perforated.

The weights of twelve animals were taken at the beginning of the experiment and again at death from which data the average weight of the animal was determined by assuming a uniform weight change throughout the experiment. Using these as *mean weight* it was possible to estimate the rate of histamine administration for these twelve dogs in terms of micrograms histamine base per kilogram body weight per minute. Reference to Table I shows that in this series of dogs, ulcers developed within two weeks or less with doses of over 1 microgram histamine per kilogram per minute while they usually did not occur when lower amounts were given. However two dogs, No. 4 and No. 12, receiving the larger doses died after 4 and 65 days of injection without ulcers, and two dogs, No. 1 and No. 18 given the smaller doses of histamine did develop ulcers. There was then no strict correlation between the histamine dose and ulcer development but in general the number and severity of ulcerations and the rapidity of their onset (as indicated by autopsy at death) were greater the larger the histamine dose.

TABLE I. EFFECT OF DOSE OF HISTAMINE

DOG NO.	WGT. (KG.)	DOSE (MG/KG/MIN.)		CONC. (MG/ML)	DAYS	RESULTS
		MIN.	MAX.			
1	16			1.5	1 wk	Perforated lesser pyloric sphincter
2	30.3			3	1 wk	Multiple ulcers of duodenum perforated esophageal ulcer
3	30			4.0	1 wk	4 duodenal ulcers 1 perforated
4	27			4	1 wk	Ulcers in esophagus only
5	4			11.3	1 wk	5 duodenal ulcers, 1 perforated 1 ulcer lesser pars intermedia
6	25			4.0	1 wk	lesions 1 ulcer 1 perforated 1 esophageal ulcer
7	6.0	22	3	2.0	Death	duodenal ulcers
8	6.4	19.3	5	3	Death	Multiple duodenal ulcers, 1 perforated 1
9	8.6	1.5	1.5	1.3	1 wk	4 acute duodenal ulcers
10	6.6	10.3	1.7	10.3	1 wk	duodenal ulcers 2 ulcers at pyloric sphincter
11	9.0	1.6	1	13.3	1 wk	duodenal ulcers, 1 perforated 1
12	7.6	11.5	1.1	6.5	1 wk	No ulcer 1 death (focal)
13	11.2	11.5	0.71	1.0	6 weeks	2 duodenal erosions
14	6.3	8.3	0.44	9.5	Death	1 duodenal erosion
15	6.4		0.46	20.3	6 weeks	Duodenitis and
16	6.6	8	0.82	20.3	6 weeks	Duodenitis and
17	7.6	7.5	0.79	13.9	6 weeks	1 duodenal ulcer
18	7.8	7.0	0.64	1.0	6 weeks	2 duodenal ulcers

In cases of histamine base

13.9 mg are equal to the injections of these dogs

Vomiting occurred in the dogs found at autopsy to have ulcers, but seldom occurred in animals which did not develop ulcers, and anorexia usually accompanied or soon followed the initiation of vomiting. Diarrhea and edema frequently occurred. Pulmonary edema or pneumonia and emphysema developed in the lungs of eight of thirteen animals examined for the condition, and these complications were probably responsible for the death of some of the dogs.

Subcutaneous inflammation was found at injection sites in the majority of the animals and was not prevented in four dogs when 100 unit of penicillin per cubic centimeter was added to the solution being injected.

**Intravenous Injection.**—Histamine was administered intravenously and continuously in sixteen dogs, in doses of from 76 to 5 mg of base per day. Seven animals were sacrificed; the remainder died during the course of the experiment. Thirteen animals developed ulcers within sixteen days or less and perforations occurred in three dogs. Of the three dogs without ulcers, one had gastric and duodenal erosions, another duodenitis, and the third exhibited no lesions.

The distribution and the type of ulcer resulting from intravenous histamine injection were similar to that following subcutaneous histamine. The ulcers usually developed in the posterior wall of the duodenum within 1 to 3 cm below the pyloric sphincter and a kissing ulcer was found on the anterior wall in four dogs. In three dogs ulcers appeared at the pyloric sphincter. Ulceration occurred in the stomachs of two dogs. One had a small lesion 0 cm above the pyloric sphincter while the other had two ulcers at a distance of 6 cm above the pyloric sphincter, two of which ulcers had perforated. This latter finding is of interest and significance. The position of these four ulcers corresponded exactly to the openings in a Rehfuess tube live, which had been put in the dog stomach for aspiration of gastric juice during an acute experiment performed the day before beginning continuous histamine injection. These ulcerations clearly indicate that the factor of mucosal injury can play a role in the production of experiment ulcers.

Animals in a minimal adequate dose of intravenous histamine is not wanted and can be seen by Table II. The data suggest that doses

TABLE II. DOSE OF HISTAMINE INTRAVENOUSLY

Dog	Dose mg	No. of ulcers		No. of perforations	No. of deaths	Remarks
		Stomach	Duodenum			
1	0	0	0	0	0	None
2	4	0	0	0	0	None
3	10	0	0	0	0	None
4	10	0	0	0	0	None
5	10	0	0	0	0	None
6	10	0	0	0	0	None
7	10	0	0	0	0	None
8	10	0	0	0	0	None
9	10	0	0	0	0	None
10	10	0	0	0	0	None
11	10	0	0	0	0	None
12	10	0	0	0	0	None
13	10	0	0	0	0	None
14	10	0	0	0	0	None
15	10	0	0	0	0	None
16	10	0	0	0	0	None
17	10	0	0	0	0	None
18	10	0	0	0	0	None
19	10	0	0	0	0	None
20	10	0	0	0	0	None
21	10	0	0	0	0	None
22	10	0	0	0	0	None
23	10	0	0	0	0	None
24	10	0	0	0	0	None
25	10	0	0	0	0	None
26	10	0	0	0	0	None
27	10	0	0	0	0	None
28	10	0	0	0	0	None
29	10	0	0	0	0	None
30	10	0	0	0	0	None
31	10	0	0	0	0	None
32	10	0	0	0	0	None
33	10	0	0	0	0	None
34	10	0	0	0	0	None
35	10	0	0	0	0	None
36	10	0	0	0	0	None
37	10	0	0	0	0	None
38	10	0	0	0	0	None
39	10	0	0	0	0	None
40	10	0	0	0	0	None
41	10	0	0	0	0	None
42	10	0	0	0	0	None
43	10	0	0	0	0	None
44	10	0	0	0	0	None
45	10	0	0	0	0	None
46	10	0	0	0	0	None
47	10	0	0	0	0	None
48	10	0	0	0	0	None
49	10	0	0	0	0	None
50	10	0	0	0	0	None
51	10	0	0	0	0	None
52	10	0	0	0	0	None
53	10	0	0	0	0	None
54	10	0	0	0	0	None
55	10	0	0	0	0	None
56	10	0	0	0	0	None
57	10	0	0	0	0	None
58	10	0	0	0	0	None
59	10	0	0	0	0	None
60	10	0	0	0	0	None
61	10	0	0	0	0	None
62	10	0	0	0	0	None
63	10	0	0	0	0	None
64	10	0	0	0	0	None
65	10	0	0	0	0	None
66	10	0	0	0	0	None
67	10	0	0	0	0	None
68	10	0	0	0	0	None
69	10	0	0	0	0	None
70	10	0	0	0	0	None
71	10	0	0	0	0	None
72	10	0	0	0	0	None
73	10	0	0	0	0	None
74	10	0	0	0	0	None
75	10	0	0	0	0	None
76	10	0	0	0	0	None
77	10	0	0	0	0	None
78	10	0	0	0	0	None
79	10	0	0	0	0	None
80	10	0	0	0	0	None
81	10	0	0	0	0	None
82	10	0	0	0	0	None
83	10	0	0	0	0	None
84	10	0	0	0	0	None
85	10	0	0	0	0	None
86	10	0	0	0	0	None
87	10	0	0	0	0	None
88	10	0	0	0	0	None
89	10	0	0	0	0	None
90	10	0	0	0	0	None
91	10	0	0	0	0	None
92	10	0	0	0	0	None
93	10	0	0	0	0	None
94	10	0	0	0	0	None
95	10	0	0	0	0	None
96	10	0	0	0	0	None
97	10	0	0	0	0	None
98	10	0	0	0	0	None
99	10	0	0	0	0	None
100	10	0	0	0	0	None

Do not give any more histamine base  
if ulcers are found in the stomach or duodenum.

of less than 1 ml rogram histamine per kilogram per minute were less effective in causing ulcers, but there was imperfect correlation between the size of dose and the onset or severity of ulceration. Reasons for this apparent lack of correlation will be discussed later.

The lungs of most of the dogs receiving histamine intravenously showed congestion, emphysema and infarcts, the latter probably caused by emboli originating from thrombi caused by the plastic tubing in the jugular vein. Usually there was some inflammation of the skin, subcutaneous tissues, and vein at the site of tube insertion.

Vomiting or evidence of vomiting was noted in eight of the thirteen dogs developing ulcer but was not observed in those animals which did not develop ulcers. Anorexia usually accompanied or shortly followed the vomiting.

*Gastric Secretory Response*—In several animals the rate of gastric secretion in response to the continuous administration of histamine was determined at

TABLE III. G. THE RESPONSE TO CONTINUOUS INTRAVENOUS ADMINISTRATION OF HISTAMINE

EXPERIMENT AND DOG NO.	TYPE OF TEST	DOSE (MG/KG/HR)	CL (PER HOUR)	TOTAL ACID (MPQ) (MCL PER HOUR)	REMARKS
I V N 10	1.	Reacid 17		130	Mortified 18 days after duodenitis
		10 mg	70	114	
		20 mg	70	122	
		30 mg	73	126	
		Reacid 53		129	
		10 mg	23	99	
		20 mg	27	122	
		30 mg	30	111	
I V N 8	1	Reacid 11		77	Death 8 days, perforated ulcer of duodenum
		10 mg	29	33	
		15 mg	44	14	
		20 mg	54	4	
I V N 16	20	10 mg	61	47	Mortified 21 days, recurrent stomach and duodenitis
		20 mg	60	11	
		30 mg	66	109	
M O N 13	10	Reacid		95	Mortified 40.5 days, due duodenitis only
		15 mg	44	107	
		25 mg	45	114	
		Reacid 87		111	
	15	10 mg	34	120	
		25 mg		109	
		35 mg	42	113	
M O N 18	10	Reacid 7		74	Regeneration, stopped within
		Reacid 8		4	
	11	10 mg	11	7	All but 1st sample stained with bile, last sample blood stained, mortal 20.5 days duodenitis only
		15 mg	1	7	
		5 mg	1	90	
		25 mg	1	15	
I V N 5	3	Reacid 34		94	Death 4.5 days after duodenitis
		10 mg	13	11	
		15 mg	40	114	
		20 mg	4	14	
		25 mg	19	14	
I V N 1	2	10 mg	54	22	Mortified 2.5 days after duodenitis
		20 mg	21	13	
		30 mg		125	
		40 mg	5	47	
		50 mg	36	137	

varying intervals after the beginning of the experiment. This was accomplished by introducing a Rehfuess tube into the stomach with the dog in a fasting state. The results of these tests are shown in Table III. It is of interest to compare these results with the values we have obtained in similar experiments upon intact dogs receiving histamine for only short periods. In these short term studies it was found that the response to a supramaximal dose of histamine varied from 38 to 109 c.c. with an average of 68 c.c. per hour and a total acidity of from 114 to 148 meq. with an average of 137 meq. per liter. In the present studies the values for the concentration of acid fall mostly within this range whereas the volumes are on the average distinctly lower than those found in the normal dog.

#### DISCUSSION

Some factors should be mentioned which partially obscure the dose-time relationship with respect to ulcer production and prevent the establishment of an exact minimal histamine dose which will cause ulceration within the period of time set in these experiments. In some cases histamine delivery was temporarily stopped by movements of the dogs which twisted the tubing. The importance of continuous administration of histamine is emphasized by the fact that in the experiment of Orndorff and co-workers ulcers were not produced by 1 mg. of histamine base per day given in ten doses at two-hour intervals, whereas we have obtained ulcers with total daily doses equal to or smaller than this by continuous subcutaneous or intravenous administration. However ulcer incidence at this dose level was low and we suspect that Orndorff and associates were not giving large enough doses of histamine. It is possible that they would have obtained some ulcers even with intermittent administration, had they given more of the drug.

Pulmonary complications, which often developed, may have enhanced the effect of histamine to cause ulceration and furthermore the results suggest that some variation occurred in the susceptibility of different health dogs to the ulcer-producing effect of histamine.

Discrepancies in the correlation between histamine dose and ulcer production due in part to the factors mentioned, make impossible any close comparison of the results obtained by subcutaneous and intravenous histamine injection. It is our opinion that the ulcers following intravenous histamine administration were smaller and less severe in opinion borne out to some extent by the finding that ulcer perforation occurred in only three animals compared to perforation in seven dogs given subcutaneous histamine. But discontinuity of drug administration occurred more often in dogs given histamine intravenously. On the basis of these experiments, we do not believe the evidence indicates that an ulcerogenic agent is released from the tissues in response to the ulcer-producing effect of histamine. On the other hand, in producing ulcers by intravenous histamine injection, the possibility that a secondary ulcerogenic agent is acting has not been completely eliminated because some inflammation did occur around the plastic tubing in the jugular vein.

We may now ask, Why does histamine administration cause an ulcer? A general statement of the possibilities may help answer this question. Irritation of the gastrointestinal tract is the end result of destruction and loss of

mucosal tissue more rapidly than it is replaced by reparative mucosal proliferation. Small ulcers do not occur because the combination of cellular resistance and reparative mechanism effectively counterbalances destructive or potentially destructive processes. Histamine must then upset this balance by increasing the destructive agency or decreasing the specific resistance of mucosal cells. It may act to slow up the proliferative processes. Finally the action may be a combination of more than one, even all of these possibilities.

The secretory and erosive properties of an acid-pepsin gastric juice are unquestioned. Histamine causes the secretion of large volumes of highly acid gastric juice as well as an increase in the secretion of pepsin although the concentration of this enzyme in histamine-stimulated gastric juice is low due to a relatively greater increase in parietal cell secretion. A limited number of experiments by Shoeb and Fogelson suggest that histamine ulcer may be delayed by the oral administration of a pepsin inactivating substance but as has been stated by one of us, although pepsin increases the destructive properties of an acid gastric juice the evidence indicates that HCl alone is sufficient to cause damage to the intestinal mucosa under proper conditions. We have found by a junction of gastric juice a continued good secretory response with respect to acid values after two weeks of histamine administration. In spite of this continued insult to the intestinal mucosa, ulcers did not always occur. This suggests that some other factor may be necessary for the development of ulceration. The possibility exists that histamine, in addition to increasing the amount of gastric juice which the mucous membrane must withstand, also decreases the resistance of the mucosa by interfering with protective mechanisms such as alkaline secretions or blood supply or with the reparative process.

Meikel and other German workers, Heinen and Krüger<sup>10</sup> have described histologic and physiologic changes in the gastric and duodenal mucosa of guinea pigs, dogs, and cat following histamine injection. The changes reported are hyperemia, edema, thrombosis, and necrosis of the mucosa and submucosal tissues with ultimate sloughing of the mucosa. These pathological changes have been ascribed to an angiotoxic action of histamine and may be due to the vasodilatation and increased permeability of the capillaries with a resulting decrease in the nutritive supply to the cells of the mucosa.

Loew, in a comprehensive review of antihistaminic drugs, cited report of a number of workers that these substances decrease or inhibit the vasodilatation and increased permeability of capillaries following histamine administration. Benadryl does not however prevent histamine ulcers in guinea pigs<sup>11</sup> or dogs.

Kahlon<sup>12</sup> has reported an adaptation of capillaries to continued histamine administration but it is possible that adequate readjustment may not occur.

Two lines of evidence bear upon the hypothesis that some factor in addition to hypersecretion operates in the production of ulcers by histamine. First we have found in experiment on intact dogs<sup>13</sup> that the maximal gastric secretory response to subcutaneous injected histamine is obtained with a dose of about 1 microgram per kilogram per minute. Yet a reference to Table I clearly reveals that continuous doses of histamine larger than this value increase the severity and rapidity of onset of ulceration. Second, Cummins<sup>14</sup> has found that ulcers are rapidly produced when 0.1 N HCl is infused into dog's stomach by

at of a fistula but that when the acidosis accompanying this addition of HCl is prevented by injecting equivalent amount of base intravenously the ulcers do not develop. This indicates the effect which metabolic disturbances may have upon the resistance of the mucosa to digestion. Hale has shown on four dogs that continuous administration of histamine does not produce acidosis. On the contrary a moderate degree of alkalosis occurred, and two of these dogs developed ulcers.

We suggest that histamine may exert a toxic effect disposing to ulceration by some disturbance of the body tissue metabolism which decreases cellular resistance to digestion and perhaps also decreases the normal repair processes, thereby increasing the vulnerability of the intestinal mucosa to the action of gastric juice.

#### SUMMARY AND CONCLUSIONS

1. Ulcers have been produced regularly in the duodenum and occasionally in the stomach of the dog by the continuous subcutaneous or intravenous administration of aqueous histamine solution in doses of one or more microgram of histamine base per kilogram per minute for periods ranging from two to sixteen days. Effective doses of subcutaneously administered histamine are in the range of those found to produce a maximal gastric secretory response in the dog.

Increasing the rate of continuous histamine administration above that which produces maximal gastric secretion increases the severity and rapidity of onset of ulceration, indicating that histamine exerts some additional action to decrease the resistance of the intestinal mucosa to the destructive effect of the gastric juice.

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mucosal than more rapidly than it is replaced by a parietal mucosal proliferation. Normally ulcers do not occur because the combination of cellular resistance and reparative mechanisms effectively counterbalances destructive or potentially destructive processes. Histamine must then upset this balance by increasing the destructive agency or decreasing the specific resistance of mucosal cells or it may act to slow up the proliferative processes. Finally the action may be a combination of more than one, even all, of these possibilities.

The necrosing and erosive properties of an acid-pepsin gastric juice are unquestioned. Histamine causes the secretion of large volumes of highly acid gastric juice as well as an increase in the secretion of pepsin, although the concentration of this enzyme in histamine-stimulated gastric juice is low due to relatively greater increase in parietal cell secretion. A limited number of experiments by Shoch and Fogelson suggest that histamine ulcer may be delayed by the oral administration of a pepsin-inactivating substance, but as has been stated by one of us, although pepsin increases the destructive properties of acid gastric juice the evidence indicates that HCl alone is sufficient to cause damage to the intestinal mucosa under proper conditions. We have found by aspiration of gastric juice a continued good secretory response with respect to acid values after two weeks of histamine administration. In spite of this continued insult to the intestinal mucosa ulcers did not at all occur. This suggests that some other factor may be necessary for the development of ulceration. The possibility exists that histamine in addition to increasing the amount of gastric juice which the mucous membrane must withstand, also decreases the resistance of the mucosa by interfering with protective mechanisms such as alkaline secretions or blood supply or with the reparative process.

Meisler and other German workers, Heinle and Hastings,<sup>10</sup> have described histologic and physiologic changes in the gastric and duodenal mucosa of guinea pigs, dogs, and cats following histamine injection. The changes reported are hyperemia, edema, thrombosis, and necrosis of the mucosa and submucosal tissues with ultimate sloughing of the mucosa. These pathologic changes have been ascribed to an angiotoxic action of histamine and may be due to the vasodilatation and increased permeability of the capillaries with a resulting decrease in the nutritive supply to the cells of the mucosa.

Loew, in a comprehensive review of antihistamine drugs, cited reports of a number of workers that these substances decrease or inhibit the vasodilation and increased permeability of capillaries following histamine administration. Benadryl does not, however, prevent histamine ulcers in guinea pigs<sup>11</sup> or dogs.

Kablson has reported an adaptation of capillaries to continued histamine administration but it is possible that adequate readjustment may not occur.

Two lines of evidence bear upon the hypothesis that some factor in addition to hypersecretion operates in the production of ulcers by histamine. First, we have found in experiments on intact dogs<sup>12</sup> that the maximal gastric secretory response to subcutaneous injected histamine is obtained with doses of about 1 microgram per kilogram per minute. Yet reference to Table I here<sup>1</sup> reveals that continuous doses of histamine larger than this value increase the severity and rapidity of onset of ulceration. Second, Cummins<sup>13</sup> has found that ulcers are rapidly produced when 0.1 N HCl is infused into a dog's stomach by

was administered intravenously. In the first experiment it was given at a level of between 129 and 166 mg of nitrogen daily per kilogram of body weight. This level had been determined from figures obtained in previous studies, in which the minimal quantity of the preparation required for nitrogen equilibrium was determined. The digest was administered in 5, 7.5, or 10 per cent solution in distilled water at a rate of 20 to 30 Gm per hour for periods of between three and five days, for each level of intake. In the study comparing oral and intravenous routes of administration, the same material (originally manufactured for intravenous use) was given orally in identical amounts (dissolved in distilled water) as three divided doses at each mealtime. It was followed by a carbohydrate beverage as a chaser. During the period of study all patients were given parenterally 500 mg of ascorbic acid and 1 cc of Bejectal daily.

The study was performed with the use of a metabolic unit staffed by special nurses and a dietitian. Representative diet were submitted for nitrogen analysis, as were all urines and stools collected during each twenty-four hour period. Methods of analysis were the same as described in previous studies.<sup>1,2</sup>

# RESULTS

*Influence of Calorie Intake upon Nitrogen Balance*—This phase of the study was carried out on five patients, at levels of calorie intake indicated in Table I. Each period of study lasted five days.

In three of the five patients, the calorie intake (exclusive of protein) was started at 1,000 calories per day and increased 500 calories at a time for three succeeding periods until the level of 3,000 calories was reached. This level

TABLE I. EFFECT OF CALORIE INTAKE UPON NITROGEN BALANCE

A	TYPE	OF	ALBUMIN			NITROGEN				
			ALBUMIN PER DAY			NITROGEN				
			MEET	EXTRA	ALBUMIN	NITROGEN		PER CENT		LA
				VENOM	EX EG	M	M	M	M	
				AMIN	MOY	PER DAY	PER DAY	PER	PER	
J. E.	5	1504	40	1744	37	162	7.6	9.1	1.5	
	5	2024	40	2264	44	186	7.9	8.9	1.0	
	5	2497	40	2537	60	166	9	9.2	-0.2	
	5	3041	210	2251	70	166	9	9	0.4	
J. F.	5	1504	14	1718	30	139	3	6.1	1.4	
	5	1997	14	2011	39	149	3	7.6	-0.3	
	5	2049	224	2273	44	149	3	6.4	+0.9	
	5	2497	224	2721	57	150	4	6.6	+0.9	
F. H.	5	1504	14	1518	22	143	0		1.0	
	5	1997	14	2011	41	143	0		-0.7	
	5	2504	214	2718	36	143	9	4	1.3	
	5	3041	214	3255	60	14		4	0.6	
F. K.	5	2013	136	2149	5	143		4	-0.9	
	5	2497	236	2733	—	143	0	0	1.0	
M. J.	5	2007	1	2107	76	15	4	5	+0	
	5	2025	144	2169	53	15	6.4	5.4	-0.6	
	5	2004	144	2148	5	15	6.4	5.0	+0	
	5	301	14	314	1	15	6.4	6.4	0	

Provided by Interchemical Corporation, name and IC hypothesis.

Prepared by Winthrop Chemical Co. at New York, N. Y. 1. Urine, mg  
 albumin, 5 mg; riboflavin, 5 mg; pyridoxine, 3 mg; calcium per lactate, 100 mg; N, 100 mg.

## STUDIES IN NITROGEN METABOLISM

### INFLUENCE OF CALORIC INTAKE AND THE ROUTE OF ADMINISTRATION OF AMINO ACIDS UPON NITROGEN BALANCE: THE EFFECT OF NITROGEN INTAKE UPON FOOD INTAKE

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DURING several years of experimental work in problems related to nitrogen balance there was frequent occasion to question certain concepts which have been generally accepted. (1) The importance of carbohydrate intake in protein metabolism has long been established. The relationship has influenced program of amino acid administration but we are not aware of any detailed study of the relationship of the caloric intake to nitrogen balance at different levels of carbohydrate consumption, the protein and fat in the diet remaining unchanged. (\*) Blum and associates and Schoff<sup>1</sup> indicated that a given protein digest produces the same nitrogen retention, regardless of whether it is administered intragastrically or orally. This finding is in marked variance with the experience of Macken and his co-workers<sup>2</sup> and with our own.<sup>3</sup> (3) Most clinicians are of the opinion that the intragastric administration of a given digest may incur a decreased food intake.<sup>4</sup>

Hence in the course of other nitrogen balance experiments, we planned a study designed to evaluate each of these three concepts.

#### METHODS

Three groups of experiments were carried out on twenty-five patients presenting various degrees of protein deficiency. Although these patients may appear to be of a heterogeneous group, they actually were not since all were protein-deficient. They were selected for these studies for two reasons: first the result obtained would apply directly to the type of patient for whom amino acid therapy is customarily indicated; second, in another investigation in which the biologic value of the same amino acid preparation used in this study was determined,<sup>5</sup> a remarkable consistency of result was observed between different types of protein-deficient patients.

A diet was selected which consisted chiefly of carbohydrate. Fat was allowed in quantities of 20 to 40 Gm per day and the extraneous oral nitrogen intake was limited to less than 500 mg per day; the latter consisted for the most part of the incomplete protein of vegetables and fruits. When the protein digest<sup>6</sup>

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Amino Acid "X" hydrochloride (for intragastric use) prepared by Interchemical Corporation, Union, N. J.



was found to be the ceiling of tolerance for most patients on a diet consisting chiefly of carbohydrate beverage. Patient J. E. appeared to have a slightly less negative nitrogen balance as the calories increased but the reverse situation was found in the next two patients, F. S. and I. R. Two (J. F. and F. R.) never attained positive nitrogen balance.

If the caloric value of protein is considered, each of the three patients mentioned received 90 calories per kilogram per day as the minimal caloric intake, which fact might explain the negative result obtained. Accordingly the reverse experiment was planned in which a 3,000 calorie diet was progressively decreased to the lowest level tolerated. One patient (T. K.) refused to cooperate after five days of the 3,000 calorie regimen and accepted an average of only 99 calories for the next five days. His average daily positive nitrogen balance of 1.0 g. (gm. per day) dropped to a negative balance of 1.0 (gm. per day). In the remaining patient (J. J.) there was no significant difference between the degree of nitrogen balance on 3,000 and 1,000 calorie regimens, but when the calories were decreased to approximately 500 per day exclusive of protein (or 1 calorie per kilogram including protein) positive balance was no longer tenable.

*Influence of Oral and Intravenous Route of Amino Acid Administration Upon Nitrogen Balance*—Eight patients were studied, four of whom had been in the previous program. Protocols of study were the same or approximate for each route of administration, shown in Table II. For all patients, that is,

TABLE II. COMPARISON OF INTRAVENOUS ORAL ADMINISTRATION OF AMINO ACIDS

PATIENT	ROUTE OF ADMINISTRATION	DAYS	TOTAL CALORIC IN AMINO ACIDS	NITROGEN			
				MO. PER		EXCRETION	BALANCE
				PER	PER		
T. K.	I.V.	3	1216	1.8	7.4	6.6	+1.2
	Oral	3	1214	1.49		5.7	2
J. E.	I.V.	3	1270	1.1	4	4.4	-3
	Oral	3	1248	1.4	4	6.7	-1.1
F. R.	I.V.	3	1233	1.43	8.0		+1.6
	Oral	3	1251	1.42	8.0	6.6	0
J. J.	I.V.	3	1113	1.5	4		+1
	Oral	3	1130	1.26	6.3	7	-4
J. W.	I.V.	3	1136	1.23	3.3	5.7	-4
	Oral	3	1113	1.1	5.3	4.3	+1.6
	I.V.	4	1110	1.23		6.6	0
	Oral	4	1110	1.23	6.6	6.6	0
J. T.	I.V.	4	1141	1.1	5	3.5	-1
	Oral	8	1191	1.1	6.3	5.7	-1.4
	I.V.	4	1176	1.2	1.5	13.2	-1.4
	Oral	4	1176	1.2	16.1		+6
M. T.	I.V.	4	1221	1.66	8	3.4	-2.1
	Oral	4	1221	1.6	1	3.8	-2.6
	I.V.	3	1144	1.66	14	3.2	-1.4
	Oral	3	1144	1.66	14.6		+6.6
V. E.	I.V.	3	1111	1.1	4	4	+3.2
	Oral	4	1111	1.01	8.1	6.7	-1.2

Provided by Interchemical Corporation and prepared on Intravenous Unit

calorie requirement to 2 calories per kilogram or less would be a boon to the problem of parenteral protein nutrition.

Our results—pronounced differences in positive nitrogen balance attained by oral in contrast to intravenous administration—differ from those reported by other investigators in man and animal for other casein digests. Branch <sup>12</sup> reported that he could produce equally good nitrogen balance whether the proteins were fed by vein or by mouth, however he used a casein digest intravenously and a natural whole protein orally. Cox compared the same preparation given by both routes in dogs, but he used serum albumin regeneration as the criterion rather than nitrogen balance. In our studies, increases of serum proteins occurred too infrequently to utilize their measurement as a reliable index.

Madden and his co-workers <sup>13</sup> however are of the opinion that both the crystalline amino acid and the protein digests are better utilized orally than parenterally.

Previous work reported from this laboratory also substantiates the result reported here. In nitrogen balance studies with an oral lactalbumin digest an average retention of 43 per cent of the nitrogen administered was observed. This percentage was considerably in excess of that noted for two other casein digests administered intravenously. These observations are important enough to merit further study. If our findings are confirmed, more emphasis should be placed on the enteral protein feeding program. For this program the protein would not have to be as completely digested; it would be less expensive to prepare and administer; it could be ingested in larger quantities; it would not have to be rendered pyrogen free; and it could be used at home. The recent marketing of a number of protein digests for oral use bears testimony to the anticipated wider application of this method of feeding.

It has been observed that patients will refuse a meal offered during or immediately after an intravenous amino acid infusion. Symth and associates <sup>14</sup> studied the influence of two different protein digests on the voluntary intake of a 3,500 calorie diet in seven patients. No significant effect was found in four patients given the amino acid orally, nor with the preparation which was a partial pork pancreas digest of casein. With a more complete acid digest of casein fortified with tryptophan, however, the depression of voluntary caloric intake exceeded the caloric gain from its administration.

In evaluating this phase of the study we excluded the caloric value of the protein in the total intake. If we had included this, it would show that actually fewer than five patients had a significant decrease in caloric intake with increase in intravenous nitrogen administration. Considered along with the fact that fifteen of the twenty patients either remained the same or showed an increase in caloric consumption, this finding suggests that a revision of this clinical concept is in order. If possible, an slight objection to the use of amino acid intravenously is easily circumvented by giving the infusion after the noon meal (it being the largest meal of the day in most institutions) and giving an additional oral feeding before bedtime.

of the amino acid preparation under investigation was determined in the human protein-deficient patient. This experiment requires the administration of the protein at carefully graded levels, starting at those known to create a negative balance. An opportunity was afforded to observe the effect of increasing the protein intake upon the voluntary ingestion of other calories, chiefly in the form of a carbohydrate beverage. Twenty such patients were available for study as presented in Table III.

Seven of the twenty patients showed a decreased voluntary caloric intake at one or more levels of amino acid intake. In three of these, there resulted a loss in weight of 1.8 to 2.0 kilograms. In eight patients, the caloric intake did not fluctuate more than 400 calories per day. In the remaining five, there was an actual increase of calories consumed. Although the decrease in caloric intake usually occurred at the peak of amino acid intake, the rise in caloric intake not infrequently occurred at this point as well. In a separate study on this group of patients, no correlation was seen between the caloric intake and the degree of positive nitrogen balance or protein regeneration.

#### DISCUSSION

The effect of carbohydrate intake upon protein nutrition was first noted by Rubner as early as 1883. He found that the protein metabolism of the fasting dog could be reduced when carbohydrate was fed. Lusk in 1890 demonstrated, in an experiment on himself, that with sudden withdrawal of carbohydrate from the diet the protein metabolism was definitely increased. Zeller<sup>1</sup> noted that not until carbohydrate intake was reduced to less than 10 per cent of the total caloric intake was protein metabolism affected. Rubner<sup>23</sup> was able to decrease caloric requirement by 33 per cent without influencing nitrogen balance. Block<sup>24</sup> found that while he maintained the protein intake of six patients at 1 Gm. or more per kilogram per day, he could reduce the caloric intake from 80 per cent to 20 per cent of basal needs and in the majority of instances still attain positive nitrogen balance. Elman<sup>25</sup> found that if the amino acid intake of dogs was adequate, the carbohydrate given as the only other source of calories could be reduced to 35 calories per kilogram per day.

These references seem to offer the explanation for our inability to achieve an improved nitrogen balance by increasing the caloric intake with carbohydrate. For this purpose, it would be much more important to increase the nitrogen intake. This observation has considerable practical import, particularly to the surgeon attempting to maintain nitrogen equilibrium during periods of enforced postoperative starvation. The previous concept has led some surgeons to prescribe at least 4,000 c.c. of 10 per cent glucose daily in order to provide the estimated minimal caloric intake deemed indispensable for nitrogen balance. Not only is this high volume of fluid believed to be unnecessary and undesirable for many patients, but if protein and salt requirements are added to it, the administration of such large volumes of hypertonic fluids might well cause unfavorable local and systemic effects. The lowering of this estimated

## INTRAPYVIC OBTURATOR NEUROTOMY FOR THE RELIEF OF CHRONIC ARTHRITIS OF THE HIP

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CHRONIC pain in the hip is almost entirely a condition of adult life and in the majority of instances is due to a chronic progressive degenerative hypertrophic arthritis (malum coxae senili) which may or may not be secondary to some incongruity of the articular surfaces arising from a condition which began in early life such as Legg-Perthes disease (osteochondritis deformans juvenilis) or a slipping of the proximal femoral epiphysis (adlescent coxa vara) or a congenital luxation or dislocation of the hip. In other instances the pain is associated with a condition of more recent origin such as Paget's disease, aseptic necrosis following a fracture or dislocation of the hip, fracture of the acetabulum or of the femoral head, or an arthritis of the infectious or proliferative type.

In addition to the pain, which is aggravated by use and relieved by rest, the movements of the hip are limited to a variable degree and the hip may be maintained in a position of deformity, especially adduction, flexion, and external rotation. It is thus evident that the patient may be seriously disabled. When confronted by a patient suffering from a condition of this type the experienced surgeon realizes that the hip is permanently damaged and that no form of treatment can be expected to restore the joint to a normal condition. He must decide whether to treat the hip conservatively or operatively.

Since operation to relieve a painful hip is a formidable procedure with a result which is too often far from satisfactory, the surgeon tries conservative treatment first and finds that his most useful therapeutic agent is a crutch or a cane. This is combined with restriction of activity, reduction in weight, a low fat diet, vitamin B complex in relatively large doses, and thyroid or parathyroid hormone when indicated. In patients with severe pain, rest in bed with or without traction may be utilized. We have tried deep x-ray therapy and large doses of strontium D without appreciable therapeutic benefit.

Not infrequently the conservative treatment fails to afford relief for the patient, he has prolonged and enforced inactivity and wishes that something more radical be done. In the past it was the custom to manipulate these hips under general anesthesia and then immobilize them in a large plaster cast in a position of abduction and internal rotation and extension. However, experience has shown that this rarely results in sufficient improvement to justify the procedure. Consequently, operation is indicated.

It has been stated that the difficulty with percutaneous intervention in these chronic painful hips is that the operation may produce a formidable and may entail a long postoperative convalescence. This is especially true of an arthrodesis of the hip which the surgeon should be leaving the patient and his family in a hospital bed weight for long time, raw, lacerated, etc. However, in these joints in which the articular surfaces are laminated, arthritis is



## SUMMARY

1 When the basal caloric intake was 50 calories per kilogram per day or higher increasing the caloric intake with carbohydrate was ineffective for improving nitrogen balance in five patients studied

The oral administration of a lyophilized amino acid preparation produced a better nitrogen balance than its intravenous administration in seven of eight patients With increased intake of protein this difference was even more apparent

3 The intravenous administration of increasing quantities of the lyophilized amino acid preparation did not consistently influence the voluntary intake of calories, principally that of carbohydrate In the majority of instances, such intake either remained stationary or was improved

We thank Dr. Mrs. Irene Maxell for the preparation of diets used in this study

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Comitz believed that the chief cause of pain and disability of the hip in arthritis deformans was the adduction contracture. He treated a series of such cases by section of the pectineus muscle and of both branches of the obturator nerve in the thigh. The operation was followed by prolonged physical therapy directed at improving the tone and power of the other muscles of the hip. This physical therapy was repeated annually in order to maintain function and postpone disability. He advised obturator neurectomy in the early stage of the disease and reported seven cases with satisfactory result. Blivenkrone Moeller reported on sixteen cases of chronic painful conditions of the hip in which the obturator nerve was sectioned inside of the pelvis by the method of Selig. In nine patients in whom there was true arthritis deformans and contracture of the adductor muscles, the results were good. But in seven cases of secondary arthritis deformans (Legg Perthes disease and adolescent coxa vara) the results were poor. There was one death in his series from pulmonary embolism. He advised that the operation be performed only in patients with true arthritis deformans and with an adductor contracture.

Cottlin<sup>10</sup> reported on sixteen patients with painful arthritis of the hip treated by Selig intrapelvic obturator neurectomy and stated that the immediate results were good in all cases but that the arthritis was progressive and pain returned in a moderate percentage of the patients.

There are also some reports of similar cases in the French literature and in these cases the operation was followed by improvement in gait and lessening of pain (Padhani, Mallet-Guy and de Mourgueses, and Sauty-Berard, and Molnau<sup>11</sup>). Tavernier<sup>12</sup> preferred the less radical procedure of section of the deep branch of the nerve including the sensory articular twig, unless there is strong adductor contracture; a considerable disability may follow complete section of the nerve.

During the past eighteen months we have performed the operation of intrapelvic division of the obturator nerve in a series of twenty patients suffering from chronic painful condition of the hip (Table I) and wish to report the results obtained in these cases.

The approach used was similar to that described by Selig. A vertical incision about an inch long is made in the lower abdominal wall along the lateral border of the rectus muscle. The lower end of the incision extends to the level of the pubic bone. The incision is carried through the superficial fascia and anterior sheath of the rectus abdominis muscle and the pyramidalis, if present, are retracted inward. With the fingers the areolar tissue and fat are stripped from the superior surface of the pubis, the fingers working outward and downward into the region of the obturator canal. The posterior sheath of the rectus is deficient in its lower portion. The intrapelvic opening of this canal is usually palpated without difficulty and then the finger is slipped outward and downward to palpate the obturator foramen. The pulsation of the artery can be felt and the nerve is hard, firm and elastic and can be rolled against the wall of the pelvis in order that it may be identified. It has been said that it feels like a pencil, but it is not just that large or hard. The head of the table is lowered and a large (1½ inch wide) ribbon or other suitable retainer is intro-

difficult to obtain and when successful the patient is handicapped by the loss of movement and may also be threatened by the possibility that the condition may involve the opposite hip. Consequently arthrodesis has largely been abandoned by us in the treatment of these conditions.

We next consider an arthroplasty. This operation has been greatly improved by Smith-Petersen, who interposes a Vitallium mold in the joint, but it is still a difficult procedure to perform satisfactorily and entails a prolonged convalescence. In our hands the results in these chronically painful hips leave a good deal to be desired. The hips are not infrequently unstable or painful or both, and the range of painless movement is usually not more than 50 per cent of normal.

Much the same may be said of the operation of cheilectomy. By this we mean the removal of the excess bone from the anterior and superior margins of the acetabulum and from around the articular margin of the head of the femur with or without the removal of diseased articular cartilage from both surfaces of the joint and the reduction in the size of the head of the femur (Murphy). In some cases Smith-Petersen's operation of acetabuloplasty which removes part of the anterior and superior portion of the acetabulum has given stable painless hips with a satisfactory range of movement. But this has occurred in the minority of our patients who have been operated upon by this method. We believe that the operation is most useful in those patients with an enlarged femoral head such as results from Legg-Perthes disease and when combined with an obturator neurectomy.

A few years ago we were impressed with the reports of the benefits to be obtained in these patients by subtrochanteric osteotomy with inward displacement and outward angulation of the shaft on the proximal fragment of the femur. We performed a number of these subtrochanteric osteotomies on patients with chronic degenerative arthritis of the hip and most of the patients were improved (Hart). However the operation entailed a prolonged convalescence and the degree of improvement was not as great as we had hoped for. So we are now performing the procedure less frequently than in the past.

For over fifteen years one of us (J. A. K.) has been performing extrapelvic section of the obturator nerves on an occasional patient with a chronic painful hip and has on several occasions combined this operation with an acetabuloplasty. Most of the patients were benefited especially by the combined procedure, however no accurate follow up records on these patients are available.

The operation of intrapelvic obturator neurectomy has the advantages that it is a relatively short and simple operative procedure once the technique of exposing the nerve has been mastered, and the convalescence from the operation is short. The technique of exposure of the nerves in the thigh was described by Stoeffel in 1910 and the intrapelvic operation was described by Seelig in 1914. However the operation is usually performed for relief of spasticity of the adductor muscles. We believe that this operation has been performed by many surgeons in this country for the relief of chronic pain and disability in the hip but we were able to find no reports in the American or English literature on patients so treated.

TABLE I—CONT'D

PATIENT NAME, SEX	DURATION OF SYMPTOMS	DIAGNOSIS	RESULTS OF TREATY	RESULTS AFTER OBTURATOR NEURECTOMY
J. W. 43, m	10 yr	Transient arthritis secondary to f. f. hip	None	Improved but still has some pain and disturbance
L. H. 42, m	3 yr	Atrophic arthritis, both hips	None	Bilateral obturator section has improved m. t. m., improved gait, pain much better but not completely relieved
X. M. 29, f	13 y	Arthritis of hip, secondary to pyogenic infection	14 operations on femur for exostosis from leg lengthening	Still worse pain although considerably improved, walks better
F. T. G. 39, m	6 y	Old septic hip right	None	Improved function of leg but feels he has lost the same pain
M. J. W. 50, f	20 y	Old septic hip right	None	Pain now less, weakness and instability in leg, feels that she is worse than before operation
K. A. 48, m	3 yr, much worse last 10 yr, deteriorating f. leg	Paget disease left hip	Conservative treatment	Very little relief of pain, complaints of weakness of leg, the more trouble sitting and controlling balance
K. H. K. 44, m	2 y	Paget disease right hip	None	Almost complete relief of pain but still pain at night, improvement gait and ease of sitting
F. Q. R. 36, m	8 y	Congenital subluxation, right hip	None	Pain much less, some loss of control sitting
M. J. 44, f	Congenital dislocation pain, only 8 yr	Congenital dislocation on both hips	None	Bilateral obturator section; pain in both hips not working but no pain when not working, no weakness or gait disturbance
M. D. 47, f	5 to 6 yr, pain worse since cup arthroplasty in 1943	Old hip fracture	Cup arthroplasty in Dec. 1943	Moderate relief of pain, leg is weaker and harder to control, but walks much better

the acetabulum. In this patient the obturator nerve could not be identified at the intrapylar operation and the bladder was inadvertently opened. This was sutured and the patient made an uneventful convalescence but the pain in the hip was not affected by the operation. In view of the experience in this case the surgeon should expect to encounter adhesions and distorted anatomy in patients who have suffered extensive fractures of the pelvis and of the acetabulum.

During the past one and one-half years we have performed the operation of intrapylar section of one obturator nerve in eighteen patients and of both obturator nerves in two patients making a total of twenty-two sections in twenty patients and these patients have been relieved for 1 month or longer. All of these patients were suffering from chronic painful conditions which affected one or both hips. In seven they varied from 3 months of pain to relief from a painful abduction of the hip to patient over 60 years of age with pain from

TABLE I

PATIENT AGE SEX	DATE OF SYMPTOM	DIAGNOSIS	PREVIOUS TREATMENT	RESULTS FOLLOWING OPERATION
C. A. 44 f	6 yr severe disability trouble th h p 7 yr	Malum osteoarthritis	Malum osteoarthritis Chl 46, no relief of pa Nose	Complete relief of pain, but difficulty in balance and con placement of calcaneus in leg
D. H. K. 40 m	8 yr	Malum coxae in left hip	Nose	Complete relief of pain, but leg given out on rise, but no great disturbance and very little limp
F. V. R. 42 m	1 yr	Malum coxae in left hip	Nose	Able to return to work some months later but no gain
C. M. O. 40 f	1 yr	Malum coxae in right hip	Appendectomy and repair of femoral hernia for this same pain	No relief of pain no calcaneus or great disturbance
I. W. 51 f	8 yr	Malum coxae in left hip	Nose	Little less pain, but still limp in cross legs, hole sitting
L. G. B. 40 m	2 yr	Malum coxae in right hip	Nose	No relief of pain, change in gait
I. H. 65 m	0 yr	Malum coxae in right hip	Nose	Little more pain, some calcaneus and no great disturbance
A. T. H. 61 m	Arthritis for many years disability in both legs	Malum coxae in both hips	Nose	Almost complete relief of pain, left leg better (leg could be fairly operated in atrophy of quadriceps); no pain in right operated hip
L. S. 49 m	1 yr	Old type femoral epiph in hip	Had osteop in hip for slipping of epiph conservative	Complete relief of pain, but trouble controlling leg in sit ting position
P. M. B. 60 f	8 yr	Traumatic arthritis fol lowing fra ture left h	Conservative	Relief of pain

duced into the wound in order to expose the nerve with a small blunt dissector the obturator nerve is stripped from the surrounding tissues, care being taken not to injure the obturator vein or artery as this may cause troublesome bleeding and make visual identification of the nerve difficult. The nerve is then lifted up, grasped with a hemostat and a section one or more inches long is excised. The wound is then closed in layers.

In adults the wound is about 4 or 5 in. in depth and the nerve is farther lateral than on the feet unless the operator has had experience with the operation. A good light should be directed obliquely downward and outward in the wound or an illuminated retractor may be used. In two bilateral cases we have used the transverse suprapubic (Pfannenstiel) incision, but we believe that satisfactory exposure is a little more difficult by this method. With either type of incision, lowering of the head of the table is helpful as the abdominal contents then tend to fall away from the nerve.

In our series of twenty patients there were no complications, but we know of one case in which the painful hip followed a fracture of the pelvis and of

TABLE I—CODY'S

TEXT AGE, SEX	DURATION OF SYMPTOM	DIAGNOSIS	PREVIOUS TREATMENT	RESULTS AFTER OBTURATOR NEURECTOMY
J H 52 M	10 yr	Traumat arthritis secondary t f of hip	None	Improve all but still has some pain no gait disturbance
L H 41 M	3 yr	Atrophic rheumat both hips	None	Bilateral obturator section has improved in t n, improved gait pain much better but not completely relieved
X M 40 F	13 yr	Arthritis rt hip, secondary to pyogenic infection	14 operations on femur for osteomyelitis from leg & given ray	Still some pain although consid- erably improved like better
F T O 30 M	6 y	Old septic hip, right	None	Improved function of leg but feels he has about the same pain
M A W 39 F	40 yr	Old septic hip right	None	Pain now has weakness and instability in leg feels that she is worse than before operation
R H 30 M	3 y much worse last 1 yr with darkening of leg	Paget disease left hip	Conservative treatment	Very little relief of pain, even pain of knee of leg th more trouble walking and con- trolling balance
A H K 81 M	3 y	Paget's disease right hip	None	Almost complete relief of pain but still pain at night im- provement in gait and ease of walking
J Q W 26 M	5 yr	Congenital subluxation os, right hip	None	Is much less some loss of control in walking
M I 49 F	Congenital dislocation pain, only 8 y	Congenital dislocation, both hips	None	Bilateral obturator section pain in both hips on walking but no pain best of walking no known gait disturbance
M B 47 F	51 & 6 yr pain worse wore hip arthroplasty in 1945	Old hip fusion	C p rtro plasty in Dec 1945	Moderate relief of pain, leg is easier and harder to on rod, but walks much better

the acetabulum. In this patient the obturator nerve could not be identified at the intrapelvic operation and the bladder was inadvertently opened. This was sutured and the patient made an uneventful convalescence but the pain in the hip was not affected by the operation. In view of the experience in this case the surgeon should expect to encounter adhesions and distorted anatomy in patients who have stiff red extensor fractures of the pelvis and of the acetabulum.

During the past one and one-half years we have performed the operation of intrapelvic section of one obturator nerve in eighteen patients and of both obturator nerves in two patients making a total of twenty-two sections in twenty patients and these patients have been observed for six months or longer. All of these patients were suffering from chronic painful conditions which affected one or both hips. In are they relieved from a source of pain which was sufficient to prevent a normal abduction of the hip in patient over 60 years of age suffering from

T M 1

P T I AGE SEX	IN VISION OF MPTD	IN VISION OF MPTD	IN VISION OF MPTD	RESULTS AFTER OPER. FOR FL. DISTURB.
C A 44 f	6 yr severe disability; trouble in hip 23 y	Unknown etiology	Heterochromia osteotomy Oct. 46, no relief of pain	Complete relief of pain, but has difficulty in balance and con- stant of calve in leg
D H K 63 m	0 yr	Malum coxae seu lux, left hip	None	(complaints of calve and that leg gives out on one, but no gait disturbance and very little pain)
F Y H 40 m	12 yr	Malum coxae seu lux	None	Able to return to work; some calve but no pain
C M C 62, f	1 y	Malum coxae seu lux, rt hip	Appendectomy and repair of femoral hernia for this same pain	Y relief of pain; no calve or gait disturbance
I W 51 f	8 yr	Malum coxae seu lux, left hip	None	I can now walk better but no relief from legs, while sitting
L O H 64 m	2 y	Malum coxae seu lux	None	Y relief of pain, no change in gait
J H 63 m	6 yr	Malum coxae seu lux	None	I am much less aware of calve and have some gait disturbance
A T H 61 m	Arthritis for max. years disability alk 11 day	Malum coxae seu lux, both hips	None	Almost complete relief of pain left leg easier (leg can be sure operation in trophy of quadriceps) no pain in right unoperated hip
A H 23, m	13 y	Old slipped femoral epiphyses, rt hip	Had osteopere- tomy H for slipping of epiphyses	Complete relief of pain; but trouble controlling leg in sit- ting position
J M H 66, f	8 yr	Traumatic arthritis fol- lowing fall from left hip	Conservative H	Relief of pain

duced into the wound in order to expose the nerve with a small blunt vector the obturator nerve stripped from the surrounding tissues, care being taken not to injure the obturator vein artery as this may cause troublesome bleeding and make visual identification of the nerve difficult. The nerve is then lifted up grasped with a hemostat, and a section one or more inches long is excised. The wound is then closed in layers.

In adults the wound is about 4 or 5 inches deep and the nerve is farther lateral than one expects unless he had had experience with the operation. A good light should be directed obliquely downward and outward in the wound or the incision, lowering of the head of the table is helpful as the abdominal contents tend to fall away from the nerve.

In our series of twenty patients there were no complications, but we know of one case in which the painful hip followed a fracture of the pelvis and of

malum coxae senilis. In one patient pain had been present for only one year but in most of them pain had been present for from six to twenty years.

The diagnoses of these patients were as follows: malum coxae senilis, old slipping of the femoral epiphysis,<sup>2</sup> traumatic arthritis following fracture of the hip,<sup>3</sup> proliferative arthritis both hips,<sup>1</sup> old pyogenic infection of the



Fig. 4 (H. H. K.)—Page disease: pain in right hip following injury. Almost complete relief of pain following resection of obturator foramina on the right.



Fig. 5



Fig. 6

Fig. 5 (C. M. C.)—Early senile coxae senilis: pain not relieved after resection of obturator foramina.

Fig. 6 (W.)—Malum coxae senilis: pain as described but unable to cross legs while sitting after obturator neurectomy.

hip,<sup>3</sup> Paget disease,<sup>4</sup> congenital subluxation of the hip,<sup>1</sup> congenital dislocation of both hips,<sup>1</sup> and a postoperative Vitallium cup arthroplasty.<sup>1</sup>

Regarding relief of pain the results were in the main satisfactory. Three patients, one with Paget disease, one with old pyogenic infection, and one with malum coxae senilis, complained that the pain was about the same as it was





Fig. 1 (A. P.)—Old displaced femoral epiphysis of right hip. Almost complete relief of pain following intrapelvic obturator neurectomy.



Fig. 2 (L. Q. W.)—Congenital subluxation of right hip. With pain on walking on the stairs during the day, improved after intrapelvic obturator neurectomy on the right.



Fig. 3 (L. M. B.)—Aseptic necrosis of left hip following fracture (right side before) almost complete relief of pain following intrapelvic obturator neurectomy on the left.

In advising the operation of obturator neurectomy for the relief of a chronically painful condition of the hip the surgeon should warn the patient that this is a palliative procedure and that it will not restore the hip to normal, but offers considerable lessening of the pain in about 80 per cent of the cases and that in most of these an appreciable improvement in the function of the hip may be expected.

## CONCLUSION

Intrapelvic obturator neurectomy is a feasible and satisfactory surgical procedure for the relief of chronic painful conditions of the hip.

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before the operation and one patient with an old septic hip complained that the pain was worse than before the operation. The other sixteen patients obtained a variable degree of relief and in most of them the relief was so great that they are glad that they had the operation performed. In nine of these the pain was completely or almost completely relieved. In the other seven there was a variable amount of relief averaging about 50 per cent and in this group the function of the limb or limbs was improved to a variable degree.

In addition to the lessening of the pain the operation was in many patients followed by an increase in the range of movement in the hips and an improvement in the gait. Some patients, however, complained of weakness of the extremity, lack of endurance in walking and difficulty in controlling the extremity especially of inability to cross the operated leg over the other actively while sitting.

In reviewing these cases we find that the effect of the operation on the hip is not specific and cannot be predicted with certainty. For instance, two of our best results were obtained in the patients with old slipped femoral epiphyses. (These are the secondary arthritis deformans in which some other surgeons have obtained poor results.) The variation in the relief from pain obtained by the operation seems to be due in part to variation in the distribution of the nerve rather than to the lesion present. In our small series we were not able to determine that the operation is especially useful in any one type of chronically painful hip and that the results are apt to be unsatisfactory in any other similar condition.

The hip obtains sensory nerves from the obturator femoral, and sciatic nerves and Ehler<sup>1</sup> stated that an accessory obturator is present in 29 per cent of individuals and that this carries sensory fibers to the hip. It is thus evident that section of the obturator nerve does not entirely denervate the hip. However, clinically we have found that the operation is followed by clinical improvement in 80 per cent of our patients.

How much of this improvement is due to paralysis or weakening of the adductor muscles we do not know. These muscles may receive some motor nerve fibers from the sciatic and some from the femoral nerve. Hence the amount of paralysis of the adductors which will follow an intrapelvic section of the way in which it is advisable to attempt to denervate the hip completely.

Since the intrapelvic section of the obturator nerve may cause almost complete paralysis of the adductors and result in weakness, instability and lack of endurance in the extremity we believe that this operation should be reserved for those cases in which adductor spasm or contracture or both, is judged to be a factor in the disability and that in most instances where an obturator neurectomy is to be performed the nerve should be exposed in the thigh at its exit from the canal and its deep or posterior branch and with it the sensory branch to the hip should be sectioned. This may or may not be combined with an acetabuloplasty. We are at present studying a series of cases operated upon in this manner.

out, except in the stages preceding death from sepsis. To be sure many patients have been observed whose spasticity has diminished in about one year to the point where it no longer prevented the use of a wheel chair. Yet many of these require treatment designed to diminish or abolish the frequent bouts of spasm. Some patients go for many hours without experiencing a single spastic movement but have from time to time severe spastic episodes. Certainly these recurring uncontrolled movements deserve attention as much as any of severe motor ties occurring in otherwise normal people. Watchful waiting—or conservatism—can only be branded as a policy of neglect. Tenotomy has not yielded a good result as nerve section and is not the procedure of choice.

Adduction is principally accomplished through the muscles innervated by the obturator nerve. The obturator nerve, a branch of the lumbosacral plexus with roots of origin in the ventral divisions of the second, third and fourth lumbar nerves, emerges from the overlying psoas muscle over the sacrotuberous joint. It courses along the lateral wall of the pelvis and enters the obturator canal. The obturator foramen is occupied largely by the two obturator muscles and is overlain by the piriformis muscle. The obturator artery usually arises from the hypogastric artery and lies beneath the obturator nerve as these structures enter the obturator canal. Within the canal, the nerve divides into two branches. The anterior branch supplies the gracilis, adductor longus, and adductor brevis muscles. The posterior branch supplies the obturator externus and adductor magnus muscles. Occasionally an accessory obturator nerve is present and supplies the pectineus muscle. The inferior portion of the adductor magnus muscle is supplied by the tibial nerve and functions chiefly in extension of the thigh.

Flexion of the thigh is largely observed by the muscles innervated by the femoral nerve. The femoral nerve with roots of origin from the dorsal divisions of the anterior primary division of the second, third, and fourth lumbar nerves, arises in the substance of the psoas muscle from the lower lateral border of which it emerges. It passes downward in the groove between the psoas and iliacus muscles to enter the thigh by passing beneath the inguinal ligament lateral to the femoral vessels and outside the femoral sheath. For the distance of approximately 1 cm. below the inguinal ligament the nerve remains as a distinct bundle then suddenly ends in profuse branching. Within the abdomen branches are given off to the iliacus muscle and the femoral artery. In the thigh, the anterior division supplies the pectineus and sartorius muscles and gives off the medial and intermediate cutaneous femoral nerves. The posterior division supplies the quadriceps and gives off the saphenous and articular branches. Just above the inguinal ligament the nerve is intimately associated with numerous blood vessels, making exposure difficult without extensive ligation of these.

In performing a section of both nerves, when skin incision is made starting 1 cm. above the inguinal ligament midway between the anterosuperior iliac and the symphyseal pubis, and extending laterally and downward to a point 1 cm. lateral to the femoral artery and 1 cm. below the inguinal ligament (see Fig. 1).

## A SIMPLE COMBINED APPROACH TO THE OBTURATOR AND FEMORAL NERVES

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IN THE course of treating patients with spasticity resulting from traumatic injury to the spinal cord, it was apparent that ambulation with braces and crutches was often thwarted by the presence of adduction spasm. Of a group of eight patients subjected to obturator neurectomy utilizing the approach described by Stoffel, six were found to have been inadequately denervated. This technique requires extensive dissection of muscles and a careful search for and identification of the various branches of the nerve. Frequently judging by my own experience, some of the more important branches are likely to be overlooked. In order to avoid this difficulty I have sectioned the obturator nerve extraperitoneally above the pelvis, usually through a short Pfannenstiel incision. The result from this procedure has been uniformly good with respect to relief of adduction spasm. In patients so treated ambulation could be pursued vigorously and adeptly. In observing attempts at ambulation in patients with severe flexion spasm in addition to adduction spasm, however, it became obvious that sharp flexion of the hip may also act as a serious impediment. Indeed, such patients find it necessary to keep their legs tied down in order to prevent being thrown to the floor during sleep. In quadriplegic patients with this type of spasm, the inability to handle a urinal adds a grave problem. Abolition of flexion and adduction spasms allows the use of a urinal between the legs and often permits removal of an irritating urethral catheter and maintenance of a dry bed. To eliminate both flexion and adduction spasm, either section of the anterior spinal nerve roots or peripheral section of the femoral and obturator nerves may be carried out.

The spasticity seen in the majority of patients with paraplegia with complete transverse lesions of the spinal cord is most frequently extensor in nature with hip flexion and abduction of the thighs, flexion at the knees, and plantar flexion. With incomplete lesions (and occasionally in proved complete lesions) the spasm is largely extensor in nature and is often associated with delayed flexor thrust which may be spectacularly severe. These patients live in constant dread of being thrown from bed during sleep. They also find that the constant spasticity keeps them physically exhausted.

The attitude of watchful waiting in the hope of spontaneous improvement is mentioned only to condemn it. No cases of spasticity even when followed as long as nineteen years after injury to the cord, have been observed to wear

## COMMENT

Because of the difficulties which follow incisions across natural skin folds and creases, it was originally felt wise not to place the incision across the flexor crease but considerable difficulty was encountered with incisions placed either inferior or superior and parallel to it. Perhaps an incision along the inguinal crease extended superiorly at its mesial end and inferiorly at its lateral end would be suitable. At any rate no annoying contractures or other difficulties have occurred in any of the patients operated upon with the incision used. Since the patients upon whom this operative procedure was used had complete anesthesia from the waist or higher there was little need to consider the possible consequences of partial denervation of the hip and knee joints, nor of the cutaneous areas supplied. Despite the fact that the primary aim was to promote better ambulation, there was often a remarkable over-all improvement in general well-being. In some patients, bladder capacity improved markedly. In other patients who had incomplete spinal cord lesions voluntary motion increased considerably. This improvement was probably due to the fact that the most severe aspects of the spasticity had merely kept the musculature from responding to voluntary stimuli. The inner surface of the thighs is one of the low threshold areas for eliciting spastic contractions, and once adduction is induced, other muscles which derive their innervation from segments of the spinal cord below the area of injury are reflexly stimulated (so-called mass reflex). With adduction being eliminated as a means of stimulating these sensitive skin areas, reflex actions are not started. Therefore the other muscles remain relaxed for long enough periods of time to make them capable of responding to voluntary impulses which previously were unable to evoke responses because they were not as strong as the reflex action. In those patients where a suspicion exists that some voluntary motion may be present resection of the femoral at the time of its division is advisable.

## SUMMARY

A simple method is described for the combined bilateral section of the obturator and femoral nerves for the adequate relief of flexion and adduction spasm in patients with paraplegia.

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The external oblique fascia is opened and the muscle is separated in the direction of its fibers. The contents of the inguinal canal are retracted medially and upward. The posterior wall is then incised bluntly 1 cm. medial to the femoral vessel. The pelvic extraperitoneal space is thus entered and dissection is carried down bluntly to the obturator foramen. Here the nerve and artery can be palpated easily. The only precaution necessary is to avoid peeling off the parietal pelvic fascia along with the nerve and artery; this error makes the dissection difficult. Retractors are placed and the blood vessels and nerve are separated. The nerve is grasped with a hemostat or a nerve hook, silver clips

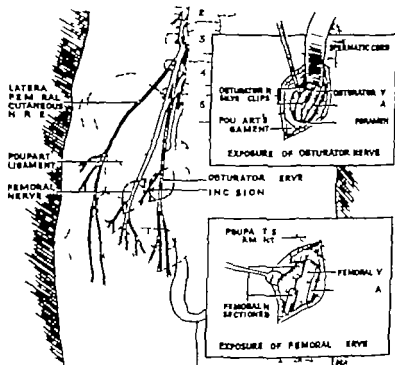


Fig. 1.—Combined approach to the obturator and femoral nerves. The skin incision is shifted to enter first over one nerve and then over the other. In the upper inset, obturator structures; in the lower inset the femoral nerve and adjacent vessels.

are applied several centimeters apart and segment of nerve is removed. The stumps of the nerve are inspected for bleeding, since occasionally the small veins in and along the nerve are not occluded by the silver clips. The skin is then retracted laterally below the inguinal ligament and the superficial fascia is incised. The fascia overlying the iliopectineus muscle is split vertically 1 cm. lateral to the femoral canal. Directly beneath, the femoral nerve can be seen and picked up. Section can be accomplished with little or no bleeding, and by flexing the thigh, resuture can be done if desired.

The wounds are closed in layers with interrupted black silk sutures.

and surrounding skin with a methacrylate polymer in order to protect the wound to prevent it from shrinking and to be able to observe it through the film. We found it difficult to measure the rate of wound healing because the polymer obscured the wound and because a bloody exudate collected under the methacrylate film. Most importantly methacrylate failed to prevent contraction of the wound and seemed to be irritating, causing in many cases fresh hemorrhage into the wound and irritation to the animals, for although they were anesthetized they immediately exhibited a protective motion with their limbs as if trying to scratch the wound.

#### METHODS

Young guinea pigs of both sexes with an average weight of 400 grams were used. They were weighed before operation and every other day thereafter until complete healing of the wound. On the day before operation, the hair of the back, sides, and abdomen was cut with clippers, followed by a depilatory. Twenty-four hours later the animals were anesthetized with sodium pentobarbital, 20 mg per kilogram of body weight intramuscularly. The skin was cleaned with soap and water followed by iodine alcohol and ether. One wound was made on the middle area of each flank, approximately 1 cm lateral to the spinal column, by a stainless steel punch. The punch ground at one end to a cutting edge had an inner diameter of 11 mm; it made a circular wound, measuring approximately 10 sq cm in area. The skin of the circular wound was dissected out with scissors, down to the subcutaneous layer with little bleeding encountered usually. Then, after applying the agent to be tested to the wound, a Lucite ring was glued tightly to the skin surrounding the wound, using methacrylate polymer solution. The ring had a thickness of 1 mm, an inside diameter of 14 mm, and an outside diameter of 16 mm. Observations of the healing of wounds with and without the ring convinced us that it prevented wound contraction largely. The surface of the ring was covered by transparent x-ray film that was cemented to it with methacrylate polymer solution, serving as a window through which the rate of healing could be observed. The rings were re-enforced with adhesive tape in order to protect them from damage by the animals. The rings did not seem to disturb the guinea pigs.

The glue was prepared by dissolving butyl methacrylate polymer and methacrylate monomer (1 gm each in 20 cc of methyl ethyl ketone; the solution was kept at 4°C).

The rate of the wound's re-epithelialization was followed by placing a piece of celluloid on the window and tracing the line of union between epithelial edge and granulating surface. Since the window was only 11 mm above the wound and since the margins of the ingrowing epithelium could be distinguished easily, the outlines could be traced accurately. The area of the tracing was measured with a planimeter according to the technique of Carrell. Wound healing expressed as the size of the healed area in per cent of the original wound. A few wounds showed slight initial enlargement.



## EXPERIMENTAL STUDY OF WOUND HEALING

### I. A NEW TECHNIQUE AND A STUDY OF THE EFFECT OF DETERGENTS AND OF AN ANTACID ON WOUND HEALING

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A NONINFECTED wound of normal skin heals rather rapidly by contraction, fibroblast growth and epithelization. With asepsis and protection of a standardized wound, healing time has been found to be quite constant.<sup>1</sup> With topical application of certain drugs, the period of healing could be shortened by a few days<sup>2</sup> and the healed wounds seemed to have the same strength and appearance as the untreated ones. We felt that shortening of the healing process was desirable and that more drugs which would accelerate wound healing should be tested. We were interested to see also whether drugs used for the treatment of peptic ulcer would affect the healing of superficial skin wounds. Lastly we wanted to extend earlier work from this laboratory on the effect of detergents on wound healing because promising clinical results had been obtained.

In the healing of a wound of the skin the processes of contraction, growth of fibrous tissue, and epithelization are apparent grossly. It is the impression of the surgeon that usually the process of epithelization is more sensitive and more easily disturbed than the other two processes, and that it needs care and protection. For this reason we have devised a simple method which measures the rate of wound healing by epithelization, excluding largely the factor of contraction.

The number of drugs in use for wound healing is great, but the subject still is controversial. A number of such substances were shown to be ineffective, namely: chlorophyll, cod liver oil, vitamins A and D, balsam of Peru, various vitamins other than C and K, irradiated petrolatum, allantoin, chloramine, urea crystals, glycerin, pectin, biotin, Biotin, urea, sulfathiazol, adenonin, and liver extracts. Other substances were discovered to disturb wound healing, namely: sulfonamides, tannic acid, riboflavin, hydrosulphosol, Hiodyne and Carbowax. Wounds dressed with petrolatum gauze and a stearate grease healed in the same time as a control. Good results have been reported with the use of thymus extract. In wound healing maintenance of nutrition of a normal metabolism and nutritional status of the body must never be forgotten.<sup>3,4</sup>

The method for wound healing used by Marshak<sup>5</sup> was tried and given up because we could not duplicate some of his findings. Marshak covered a wound

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TABLE I. A. RATES OF HEALING OF WOUNDS WITH VARIOUS DETERMINANTS

TREATMENT	NO. OF WOUNDS	C. RATES OF HEALING OF WOUNDS (POSTOPERATIVE %)												AGE
		1	2	3	4	5	6	7	8	9	10	11	12	
A. 1% iodine	11	110	150	155	160	160	160	160	160	160	160	160	160	110
B. Control	11	30	90	110	160	160	160	160	160	160	160	160	160	117
C. 1% sodium iodide	21	90	180	1070	100	1680	3430	4750	6610	680	807	99117	1002	210
D. 1% sodium iodide	8	-630	470	40	40	2330	3090	6950	7390	8141	1007			109
E. 1% sodium iodide	4	110	110	380		5180	6640	9120	9762	1001				9
F. 1% sodium iodide	10	80	1230	2340	440	5390	5630	8290	9265	1005				95
G. 1% tetraiodide	4	430	1630	1710		3590	5790	7150	7390	8772	9761	1001		119
H. 1% sodium iodide	3	610	3010	3650	470	3130	3390	6090		8361	100			107

The different series of experiments performed were compared for statistically significant differences by the chi square test (Fisher) using a 5 per cent level of significance. Under results, we refer to this analysis, when differences are called statistically significant. Most reliance was placed on the proportion of animals showing 80 per cent healing of the wounds on the eighth day for the following reasons: healing was definitely progressive on that date when the results were compared it became evident that on the eighth day differences between the series of experiments were most pronounced when certain drugs obscured the wounds so that daily readings of the rate of healing could not be obtained, the windows over the wounds had to be removed since this could not be done repeatedly without disturbance of the wounds, it was convenient to choose the eighth day for removal.

#### EXPERIMENTS

The detergents used were of the anionic cationic and nonionic type, with sodium lauryl sulfate (Difol) tetramethylammonium-hydroxide (Triton NP) and alkyl-dimethyl-benzyl-ammonium-chloride (Zephiran) chosen from each — — — — — made in this —

The rate of healing of control wounds was found to be the same, whether an animal had an untreated wound on one flank and a treated faster healing wound on the other flank, or whether both wounds were treated or untreated. This showed that the healing process of one wound did not influence that of the contralateral side.

Wounds with low-grade infections healed as well as clean, noninfected wounds. Animals with distinctly infected wound were discarded. Untreated controls were run throughout the duration of this work, in order to eliminate possible changes in rate of healing due to extraneous factors, or due to nutritional deficiencies. All animals were fed the same diet of cabbage lettuce alfalfa, and oats. Following completion of healing of the wounds, the animals were etherized and exsanguinated, and hemoglobin, red blood cell count, and total proteins were determined. After observing wound healing in Controls A and B and after having observed all animals not operated on, but shaved, given anesthesia, weighed, and fed the same as the operated animals, it was found that variations in body weight, red blood cells, hemoglobin, and total proteins were insignificant.

#### RESULTS

The average rate of healing of untreated control wounds (Table I, Controls A and B) was inconsistent during the first six postoperative days: so far that a progressive process of healing was not evident. At the seventh to eighth day this inconsistency disappeared and healing became progressive. This is demonstrated by Controls A which, on the fourth postoperative day showed an average rate of healing of only 16.6 per cent with variation of -28.6 to 50 per cent. No significant increase in the rate of healing was noted until the eighth postoperative day.

case. The sodium carboxymethylcellulose increased the rate of healing significantly with 100 per cent healing of all animals on the ninth postoperative day and 80 per cent healing before the eighth day. Series J (sodium carboxymethylcellulose and magnesium oxide) and K (sodium carboxymethylcellulose, sodium bicarbonate and magnesium oxide) also displayed marked increases in the rate of healing over Controls A and B. In Series J 100 per cent healing of the animals occurred in 8 days, and 80 per cent before the eighth day. In Series K, 100 per cent healing occurred on the ninth day and 80 per cent on the eighth day. Statistically there was no significant difference between the effects of the different antacids, but we feel that Series J with 1.8 per cent carboxymethylcellulose and 0.6 per cent magnesium oxide gave the best results.

A summary of all results on the eighth day is presented in Table III. The spread in the range of the rate of healing is presented in the first column; it was wide in the control and with 1 per cent sodium lauryl sulfate in water or in ointment and it was distinctly smaller, that is, healing was more uniform, with all detergents and with all antacids in methylcellulose.

The mean rate of healing (Column 2) was high, that is, above 80 per cent for 1 per cent and 0.6 per cent sodium lauryl sulfate in methylcellulose and for all three antacids.

In the case of 1 per cent sodium lauryl sulfate in methylcellulose the data are even better than apparent in Table III, because 80 per cent healing was attained on the seventh day at least; likewise in the case of the antacids, healing on the eighth day was well above 80 per cent in Series I and J. In Experiment J the wounds were measured on the seventh day (not on Table III) and showed

TABLE III. PERCENTAGE WOUNDS HEALED EIGHTH DAY

PREPARATION	1 OF 10 PER CENT HEALING	MEAN OF PER CENT HEALING	J WOUND WITH 10 PER CENT OF WOUND MEAN OF TOTAL OF WOUNDS	
			WOUND WITH 10 PER CENT OF WOUND MEAN OF TOTAL OF WOUNDS	WOUND WITH 10 PER CENT OF WOUND MEAN OF TOTAL OF WOUNDS
A Control	21.4	51.0	1/1	1
B Control with methylcellulose	10.3	46.0	0/11	0
C 1% sodium lauryl sulfate in H <sub>2</sub> O	90.91	56.1	0/1	0
D 1% sodium lauryl sulfate in ointment	37.70	6	0/15	0
E 1% sodium lauryl sulfate in methylcellulose	0.690	61.7	4/4	0
F 0.6% sodium lauryl sulfate in methylcellulose	66.691	97.6	5/10	3
G 1% tetrasodiumborate in methylcellulose	69.77	71.5	0/4	0
H 1% alkyl dimethylbenzyl ammonium chloride in methylcellulose	61.70	66.0	0/3	0
I 1% sodium carboxymethylcellulose	77.9	90.0	6/5	0
J 1% sodium carboxymethylcellulose 0.6% sodium bicarbonate	90.100	77	7/10	3
K 1% sodium carboxymethylcellulose 2.2% sodium bicarbonate 0.6% sodium lauryl sulfate	70.00	61	4/10	0

In Control A and B Table I the average time of complete healing was 116 and 117 days, respectively and 80 per cent healing was observed in both on the tenth to eleventh day. There was not statistically significant difference between Controls A and B.

In Control A the wounds were untreated, while in Control B 2 per cent methylcellulose solution was applied to the wounds. This solution was selected as a base for drugs for its low absorbability and its transparency and for staying in contact with a wound for a relative long period of time. Aquaphor ointment base (U.S.I. ointment No. 11) was found unsatisfactory because it concealed the wound. The use of water as a solvent was unsatisfactory as absorption and evaporation of the water could not be controlled. After one series with a single application of 1 per cent sodium lauryl sulfate in water another series was performed with reinstillation of the watery solution through the window every other day. Since the results were practically the same, they were added together as Series C which was not significantly different from the controls. Neither did 1 per cent sodium lauryl sulfate in Aquaphor ointment show a pronounced effect on healing (series D).

Series E, with 1 per cent sodium lauryl sulfate in methylcellulose, showed complete healing in 9 days and 80 per cent healing in 8 days. The statistically most significant increase in the rate of healing with detergents was noted in Series F using 2 per cent sodium lauryl sulfate in methylcellulose, with 100 per cent healing in 8.5 days and 80 per cent healing in 7 days. Tetramethylammonium-hydroxide (Series G) and alkyl-dimethyl-benzyl-ammonium-chloride (Series H) both in methylcellulose did not show significant effects on healing rate.

On studying the average percentage rate of healing with antacids (Table II) it was found difficult to measure the size of the wounds every day because the antacid solution or suspension were cloudy. Therefore, the degree of healing was determined on the eighth day.

In Series I (sodium carboxymethylcellulose) an additional control was run with an untreated wound on one side of the animal and 3 drops of a 1.8 per cent sodium carboxymethylcellulose solution on the other in order to determine whether a gradual improvement of our operative technique might have changed the rate of healing of untreated wounds. It was found that this was not the

TABLE II. A. EARLY PERCENTAGE RATE OF HEALING WITH ANTACIDS

TYPE OF AGENT	NO. OF WOUNDS	PER CENT RATE OF HEALING OVER NUMBER OF WOUNDS HEALED COMPLETELY (OCTOBERATIVE YEAR)				
		8	10	11	12	13
I 1.8% sodium carboxymethylcellulose	8	90.0	100.0			
J 1.8% sodium carboxymethylcellulose 0.9% magnesium oxide	10	97.5	100.0			
K 1.8% sodium carboxymethylcellulose 0.23% sodium bicarbonate, 0.23% sodium lauryl sulfate	10	81.0	90.0			
A. Control	4	81.0	70.0	79.2	90.7	99.1

## SUMMARY

A simple technique is described for the study of the epithelization phase of wound healing with which the contraction phase of healing is eliminated largely.

Sodium lauryl sulfate and sodium carboxymethylcellulose, a new antacid, in a methylcellulose base showed a significant increase in the rate of healing.

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90 per cent healing already. Although statistically there was no significant difference between the effect of the various detergents, we feel that per cent sodium lauryl sulfate in methylcellulose was the best combination. There is no significant difference between the results with 2 per cent sodium lauryl sulfate (Series F) and 1.8 per cent sodium carboxymethylcellulose with 0.6 per cent magnesium oxide both in methylcellulose base.

#### DISCUSSION

According to Hartwell, epithelization takes place through ameboid movement into the wound of epithelial cells from the surrounding epithelium. Epithelization is completed by union of extension membranes growing from the edges of the wound. According to Hartwell, the formation of such membranes is dependent on the presence of a supporting base suitable for epithelial cell movement. This base is a factor for the support and advance and for the time of union of the epithelium from the edges of a wound. The presence of an unsuitable base is probably one of the causes of delayed wound healing and it may be responsible in part for the formation of indolent wounds.

Another factor in wound healing is pH. Heterolysis seems to depend mainly on action of leucocytic enzymes which, at alkaline reaction, digest dead tissue but which do not attack living cells or unchanged connective tissue fibers. This heterolysis of dead tissue permits the removal of barriers of dead tissue to the extension membrane and allows for the ameboid activity of the epithelial cell. Mersel and McClellan found that wound benefited more from an alkaline pH than from an acid one, but we are aware of evidence that acid or a pH between 6 and 8, is favorable to wound healing.

The significantly increased rate of epithelial healing seen in our experiment with the detergent sodium lauryl sulfate in methylcellulose base can be attributed in part to its alkaline reaction, and to its spreading by lowering surface tension. The methylcellulose which is most series as a base for keeping the detergent in moist contact with the wound for a sufficient period of time and it may constitute a supporting base suitable for epithelial cell movement, which helps the expansion of the epithelial membrane. The effect of lowered surface tension by itself on wound healing is unknown, but it may play a role in the process of ameboid epithelization.

The significantly increased rate of healing seen in our experiment with sodium carboxymethylcellulose plus sodium bicarbonate or sodium carboxymethylcellulose with 0.6 per cent sodium bicarbonate may be attributed to the two factors just mentioned. First these substances give an alkaline pH, and second, carboxymethylcellulose itself may have served as a supporting base.

These studies are continued with sodium carboxymethylcellulose in patients with peptic ulcer and with antireticulocyte serum on wound healing in guinea pigs.

one consisted of twenty five patients who were used as the control group. These patients received no medication other than an occasional 5 gr of Aspirin. The second group of patients were given oral diethylstilbestrol in a dosage of 5 mg the afternoon before surgery and then 3 mg twice daily through the fifth or sixth postoperative day. Sodium bromide in onset dose of 2 Gm the afternoon before operation, and 1 Gm three times daily thereafter was given to patients in the third group. The fourth group was treated by hypodermic injections of estrogen once daily (1 mg or 10 000 units of Estrone) beginning on the day before surgery.

After the completion of this study our attention was drawn to a recent report by Higgins in which he recommended the preoperative use of stilbestrol in young hypospadias patient until they are unable to have an erection. Accordingly we added a fifth group of twenty five patients to our series, giving them 3 mg of stilbestrol twice daily for three to seven days before surgery and continuing until the fifth postoperative day.

## RESULTS

Out of the 120 patients reported here in five equal groups, the number of erections per patient for a five-day period, starting with the day of surgery and continuing through the fifth postoperative day varied from 0 to 10 with a mean average of 1.8 erections per patient. Table I compares the total number and average number of erections in the five groups.

TABLE I

GROUP	TOTAL ERECTIO NS	MEAN OF ERECTIO NS	PERCENT OF TOTAL ERECTIO NS	MEAN OF ERECTIO NS
I Control	12	0.24	1.0	1.41
II Diethylstilbestrol (started the afternoon before surgery)	135	2.7	75	1.09
III Sodium bromide	124	2.48	71	1.02
IV Estrone	132	2.64	94	1.1
V Diethylstilbestrol (started the day before surgery)	30	0.6	21	0.44

It is readily apparent that the patient receiving oral diethylstilbestrol several days before surgery had a great diminution in the number of erections compared to the patient in the other groups.

The age (16 to 30 years), weight (127 to 220 pounds), or race of the patient seemed to have little relationship to the frequency of erections. The patient classified as being an emotional status had the greatest number of erections (Table II).

TABLE II

EMOTIONAL STATUS	TOTAL ERECTIO NS	MEAN OF ERECTIO NS	PERCENT OF TOTAL ERECTIO NS
Stable	17	0.34	1.41
Normal	111	2.22	59.9
Labile	7	1.43	5.6



# THE EFFECTIVENESS OF DRUGS IN PREVENTING POSTOPERATIVE PENILE ERECTIONS

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THE pain, wound separation and hemorrhage occasionally seen in patients undergoing penile surgery are interesting complications to both patient and surgeon. If erections could be stopped or diminished during the immediate postoperative period these complications could be reduced to a minimum. When this trial was begun a review of the literature covering the past ten years showed but a single reference to this subject. Christopher's recommendation to use a humoral di-

## METHOD

In conducting this study it was decided to evaluate the effectiveness of sodium bromide, oral diethylstilbestrol and hypodermic estrone on young male patients who were to have circumcisions. This work was done at an Army Station Hospital located at a Port of Embarkation. The patient used in the study was enlisted Army personnel. All patients were hospitalized to allow for close observation, daily penile length and strict control in the administration of the appropriate drugs.

Patients were admitted to the hospital the day before surgery and were not discharged until the fifth postoperative day or later. We carefully interviewed each patient daily as to the number, severity and duration of penile erections during the preceding twenty-four hours. The results were tabulated on master chart. All surgical complications were noted and recorded. The patient's age, weight, degree of phimosis and emotional status were charted.

The operative procedure of circumcision was standardized by us to obtain further uniformity. The method described by Pugh, Orr and Christopher was used in this series of cases. Anesthesia was obtained by dorsal nerve block with 1 per cent procaine and local infiltration when necessary. A few patients were given a caudal block type of anesthesia (30 cc. 1.2 per cent procaine). In this series no dressings were used, the patients being instructed to sponge the wound with 1 per cent boric acid solution every thirty to sixty minutes during the day of operation. This usually resulted in a dry and painless wound after a few hours.

A total of 15 circumcisions were done by us in this series. Reported here are 13 of these cases, divided into five study groups. The remaining 2 were eliminated from the series because of mixed meditations or incomplete follow-up.

We originally divided our patients into four groups of twenty-five patients each. Patients were assigned at random to the various study groups. Group



Complications encountered in the 157 cases of circumcisions were on the whole minimal. Of thirty patients given bromides, one had nausea and three had nausea and vomiting (one of which had such severe vomiting that the drug was discontinued). Only one of the fifty-eight patients given oral diethylstilbestrol had nausea. The high incidence\* of gastric reactions reported in other series of stilbestrol therapy was not substantiated in this group of male adults on relatively large doses (10 mg daily).

There were five cases with mild postoperative bleeding from the circumcision wound and two with severe bleeding, necessitating ligation of the bleeders. One patient had a severe wound separation about ten days postoperatively due to frequent and intense erections which came on after the stilbestrol therapy had been discontinued on the seventh postoperative day. Two other patients had small partial wound separations. One patient had a persistent subcutaneous infection of the penis manifested by pain, tenderness, and edema that required incision and drainage on the ninth postoperative day.

#### CONCLUSIONS

1. Postoperative comfort can be improved, and complications reduced in patients undergoing circumcision by minimizing erections with the use of adequate pre- and postoperative stilbestrol therapy.

In plastic operation or amputations of the penis, prophylactic stilbestrol therapy to minimize erections would seem to be particularly indicated.

#### ADDENDUM

As the completion of this study involves a published report which presented his results controlling postoperative penile erections with stilbestrol, Dr. experimenters based dosages of 4 mg daily controlled 50 per cent of erections, and dosages of 6 mg daily controlled 75 per cent of erections. (Erections were classified as uncontrolled if the patient had average of one or more erections per twenty-four hours for the five day period.)

In our series the patients who received 6 mg of stilbestrol twice daily beginning the evening before surgery had 75 per cent fewer erections than the control group. Those receiving stilbestrol 6 mg twice daily for at least three days preoperatively had only 31 per cent as many erections as the control group.

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on pulled and arose from the anterolateral part of the liver about three quarters of the way to the right lobe and the remaining one quarter of the mass extended across the left lobe (Fig. 1). By incising the tumor the gall bladder and the hepatic hilum were exposed lying just posterior and inferior to the lowermost line of attachment of the tumor. By traction downward on the tumor the posterior border could be visualized. After complete freeing of the tumor and adjacent liver from all adhesions the anterior and lateral abdominal parietes, the resection of the tumor was begun in first placing a double row of mattress sutures of silk through the full thickness of the liver to the margin of the tumor on the right and drawing the liver outward over the half of the incision between these sutures. By drawing the margin of the tumor thus over the peritoneum to control bleeding about midway of the incision. After the right half of the tumor had been freed in this manner it was removed and the incision began the resection on the same side the left

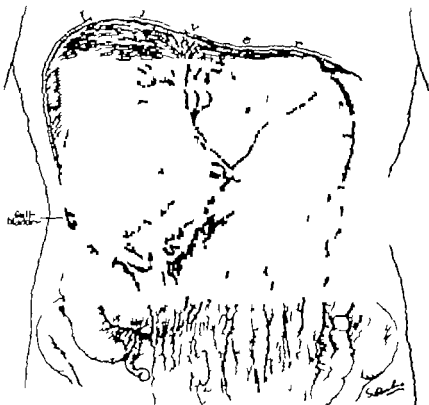


Fig. 1. Illustration showing the relation of benign adenoma of liver to gall bladder in dog.

and all over the right lobe and was completely removed (see large illustration margin of normal liver mass). Traction on the tumor greatly facilitated the placing of sutures and the exposure of the hilum. This maneuver repeated and just to the internal biliary duct. The gall bladder was held in place by the lower margin of the liver from the posterior as the upper and lower margins of the liver were exposed. The common duct was not disturbed and so long as the tumor the hepatic hilum had been freed in respect to the large tumor. Several pieces of gauze were placed over the raw surface of the liver to control seepage in case

**Laboratory Studies**—The urine as against the hemoglobin as 11 Gm. per cent, and the leucocyte count was 8,200 with normal smear. Merochrome test for syphilis as negative. Further blood studies showed acroprotein nitrogen 31 mg. per cent; fasting blood sugar 85 mg. per cent; chlorides 103 meq. per liter;  $\text{CO}_2$  combining power 27 meq. per liter; bilirubin less than 0.8 mg. per cent; amylase 73 mg. per cent; reducing substance alkaline phosphatase activity 5.0 Bocksky unit; serum protein 8.0 Gm. per cent; th. albumin 5.1 Gm. per cent; and globulin 2.7 Gm. per cent. Lactar function test showed bromsulphalein 0.9 mg. per cent retention per 30 minutes; hippuric acid 1.015 Gm. excreted in one hour; cephalin flocculation negative; thymol turbidity 0.3 unit.

A roentgenogram of the chest showed no abnormalities. On ray examination of the abdomen after the ingestion of barium meal there was seen a large rounded shadow in the right upper quadrant with marked displacement of the stomach and duodenum to the left (Fig. 1). Intra-cine psychograms showed the kidney to be normal in size, shape and position. There was no displacement of the right kidney by the mass which lay anterior to it. On cholecystography there was no concentration of the dye in the gall bladder.

The preoperative diagnosis was hepaticoma of unknown etiology, possible benign tumor of liver; chronic cholecystitis and cholelithiasis.



Fig. 1.—Roentgenogram of abdomen after barium meal showing displacement of stomach and duodenum to left by hepatic tumor in right lobe of liver (indicated by arrows).

**Operation (W. P. L.)**—Under gas-oxygen ether anesthesia, right subcostal incision placed and the peritoneal cavity entered. There were dense vascular adhesions between the omentum, the anterior abdominal wall, and a large rounded tumor which extended from the lower border of the right lobe of the liver. The omental attachment to the tumor was divided and the hepatic flexure of the colon was mobilized. A specimen of the tumor was obtained for biopsy and the report on the frozen section was liver cell carcinoma. After extending the subcostal incision from the midline and by dividing the falciform ligament adequate exposure of the tumor was obtained. This was about 20 inches in diameter with

On section the cut surface tan color resembled liver. There was no bile staining. No areas of necrosis were found and nowhere did the capsule appear to be invaded.

On microscopic examination of sections from different parts of the tumor similar histologic picture was seen. There was delicate fibrous capsule which was scarred in areas. The parenchyma was composed of almost normal appearing liver tissue with polygonal cells resembling normal hepatic cells (Fig 4). The cells of rosette cord which accumulated with one another leaving sinusoidal endothelial lined spaces between them? accumulations of bile pigment were seen as in the sections. Central veins were seen in some areas and portal areas were quite evident but bile ducts were completely absent. The parenchymal cells were regular in size with high perichromatism and no mitotic figures were seen. There was no stain of the capsule.

*Diagnosis*—Adenoma of liver hepatic cell type.

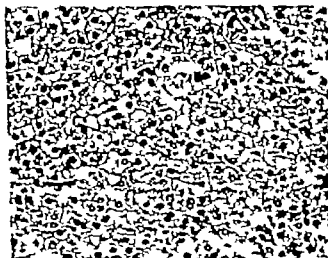


Fig 4.—Photomicrograph (X358) showing histologic detail in benign adenoma of liver (H11).

#### DISCUSSION

In recent years there has been increasing interest in surgical resection of tumors of the liver. In this case Shumaker<sup>1</sup> in 1941 successfully removed an angioma of the left lobe and Pickrell and Clay<sup>2</sup> in 1944 developed a technique for total left lobectomy of the liver applying it successfully in three cases.

Warren in 1941 found thirty-three instances of resection of well-differentiated adenoma of the liver in the world literature with a postoperative mortality of 9 per cent. He added three cases from the Cincinnati General Hospital. Herndon<sup>3</sup> reported a case in 1946, and in 1947 two additional cases were reported by Duckett and Montgomery.

Earlier reports are concerned chiefly with wedge-resection of tumors of the left lobe or with lesions having a pedunculated attachment. Notable exceptions are the cases reported in 1923 by Turner<sup>4</sup> and by Wright.<sup>5</sup> The majority of successful resection of primary tumors of the liver of a sessile nature involving the right lobe has been reported within the last five years. The present case demonstrates the feasibility of removal of a large sessile adenoma with a large pedicle just above the lesser curvature and extended deeply into both right and left

and the mentum was brought up this way. A cigarette drain was placed to Marleen's pouch and the abdominal serosa then closed layers with interrupted silk sutures.

Course.—The patient received total of 2,000 cc of whole blood during the operative procedure and in the immediate postoperative period. She had low grade fever for the first few days after operation but this subsided. Penicillin in doses of 320,000 units daily was given for ten days. She remained on high carbohydrate low fat diet. The drain was mobilized easily and was not completely removed until the tenth postoperative day. The wound healed per primam and recovery was uneventful.



Fig 2.—Photograph of surgically resected hepatic tumor (R.H.) weight 925 Gm.

On the eighth postoperative day blood studies were repeated with the following results: aspartate transaminase 29 mg per cent, fasting blood sugar 85 mg per cent, chloride 103 meq per liter,  $\text{CO}_2$  combining power 24 meq per liter, bilirubin 4.8 mg per cent, serum protein 7.3 (60 per cent with albumin 4.4 Gm per cent and globulin 2.9 Gm per cent), serum amylase 1.25 mg per cent, reducing substance, cholesterol 153 mg per cent, alkaline phosphatase activity 4.3 Bodansky units. Liver function tests were repeated and showed bromsulphalein 2.3 mg per cent retention 30 minutes, hippuric acid 0.85 Gm excreted in one hour, cephalin flocculation negative and thymol turbidity 2.7.

The patient was discharged on the twelfth postoperative day. She has been followed for five months in the outpatient department and remains in good health with no evidence of recurrence of the tumor and no signs of hepatic damage.

Pathologic Examination.—The specimen consisted of an encapsulated mass measuring 15 by 12 by 7 cm. and weighing 925 Gm (Fig 2). The mass was quite firm. The capsule was roughened by adhesions in numerous areas but was intact except at the site of biopsy.

By Dr. Mitchell Miller

## PSEUDOCELLULITIS: A REACTION TO PENICILLIN IN PEANUT OIL AND BEESWAX

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THE ease and convenience of administering penicillin in a menstruum of peanut oil and beeswax by daily intramuscular injection as well as its proved efficacy in the treatment of infection caused by penicillin-sensitive organisms, have prompted its wide use for a variety of infections.

This report was stimulated by the observation of four instances of severe delayed local reactions to this drug. The reactions appeared seven to ten days after the first injection. They were characterized by the rapid appearance of tense painful swelling of the entire buttock associated with severe tenderness, generalized malaise and a temperature up to 101°. In addition there was an erysipeloid skin eruption circular in shape the center of the circle corresponding with the site of the needle puncture of the original injection. The central zone of this eruption was somewhat evanescent and the edge of the eruption sharp and raised. When injection had been given in both buttocks the lesion began in one and was followed within twelve to thirty-six hours by a similar but less marked reaction in the opposite buttock.

In every instance the lesion reached its peak in forty-eight hours and then receded spontaneously within seven to ten days, leaving merely a small residual tender nodule in the subcutaneous tissues along the track of the original needle puncture. This nodule then slowly receded in a further fifteen to forty-five days.

In every instance constitutional symptoms occurred, consisting of malaise and fever. In two there were also joint pains, urticaria and rhinitis.

The initial appearance of these lesions, most suggestive of severe cellulitis of the entire buttock, complicated by erysipela spreading from the site of the injection. However the delay in the development of the lesion, the rapid improvement of an identical lesion in the other buttock when injections have been given bilaterally, the subsidence of the reaction without specific treatment and the absence of either suppuration or necrosis of tissue discount the possibility. The delay in the reaction at rarity and lack of necrosis also exclude the possibility of simple local irritation.

One must conclude that these are allergic reactions. In addition to the fact that infection and primary irritations are excluded for the reasons already given positively even for this point of view includes the following: (1) the known role of penicillin as an allergen; (2) the appearance of the reaction only after a latent period of seven to ten days in each case; (3) the association of other known manifestations of serum sickness such as urticaria and joint pains, with the local reaction in two of the patients.



lobes. This patient had undergone two previous laparotomies but no attack on the huge tumor had been essayed. Since our biopsy showed the lesion to be a benign adenoma of the hepatic cell type we attempted resection and were able to remove the encapsulated tumor completely. The result has been quite satisfactory.

In Warui's collected series there was a recurrence rate of 21 per cent although these tumors had been classified histologically as benign adenomas. This evidence supports the view that malignant hepatomas and malignant cholangiomas not infrequently have their origins in pre-existing adenomas.<sup>4</sup> Accordingly radical resection of these lesions is definitely indicated.

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## PSEUDOCELLULITIS, A REACTION TO PENICILLIN IN PEANUT OIL AND BEESWAX

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THE ease and convenience of administering penicillin in a menstruum of peanut oil and beeswax by daily intramuscular injection as well as its proved efficacy in the treatment of infection caused by penicillin-sensitive organisms, have prompted its wide use for a variety of infections.

This report was stimulated by the observation of four instances of severe delayed local reactions to this drug. The reactions appeared seven to ten days after the first injection. They were characterized by the rapid appearance of tense painful swelling of the entire buttock associated with severe tenderness, generalized malaise and temperature up to 10°. In addition there was an erysipeloid skin eruption circular in shape, the center of the circle corresponding with the site of the needle puncture of the original injection. The central zone of this eruption was somewhat vacuolated and the edge of the eruption sharp and raised. When injections had been given in both buttocks the lesion began in one and was followed within twelve to thirty-six hours by a similar but less marked reaction in the opposite buttock.

In every instance the lesion reached its peak in forty-eight hours and then receded spontaneously in seven to ten days, leaving merely a small residual tender nodule in the subcutaneous tissues along the track of the original needle puncture. This nodule then slowly receded in a further fifteen to forty-five days.

In every instance constitutional symptoms occurred consisting of malaise and fever. In two there were also joint pains, urticaria and rhinitis.

The initial appearance of these lesions is most suggestive of severe cellulitis of the entire buttock complicated by erysipela spreading from the site of the injection. However, the delay in the development of the lesion, the rapid superinfection of an identical lesion in the other buttock when injection have been given bilaterally, the burden of the reaction without specific treatment and the absence of either suppuration, necrosis or tissue sloughs, thus preclude the delay in the reaction, its rapid and lack of necrosis also exclude the possibility of simple local irritation.

One must conclude that these are allergic reactions. In addition to the fact that infection and primary irritation are excluded of the reasons already given, positive evidence for this point of view includes the following: (1) the known role of penicillin as an allergen; (2) the appearance of the reactions only after a latent period of seven to ten days in each case; (3) the association of other known manifestations of serum sickness, such as urticaria and joint pains, with the local reaction in two of the patients.

Though skin tests were inconclusive, failure to elicit positive skin reactions does not argue against the probability of an allergic reaction as negative skin tests are common in other drug allergies. Thus, in a series of twenty-five patients with the induced urticarial reaction to penicillin, only ten gave a positive delayed skin test to penicillin. Immediate tests were negative throughout.

#### CASE REPORTS

**CASE 1**—A 20-year-old white woman had paronychia of the left middle finger of ten days' duration and whitish lesions of the right fifth finger of 8 days' duration. The lesions were drained by pushing back the paronychia with 200,000 units of penicillin in oil and 25 were given intracutaneous each buttock on alternate days. The lesions subsided in 8 days.

Eight days after receiving the first injection of penicillin the patient noted tenderness and swelling of the right buttock. Temperature was 101° F. A small but less severe swelling of the left buttock appeared the next day. At the same time drainage recurred from the paronychia of the left middle finger. This cleared after incision. Examination revealed typical lesions, just described. The lesion of the right buttock was about seven centimeters in diameter and that on the left about five inches in diameter. These lesions subsided spontaneously in ten days leaving indurated nodules about 1 cm. in diameter at the site of the needle puncture in both buttocks. These nodules resorbed completely in four weeks.

The patient gave no personal allergic history. Her mother had angioneurotic edema for many years. The patient's only previous and unsuccessful contact with penicillin had been an intramuscular penicillin for one or two months before the present reaction. Her father and sister had poliosis.

Skin testing with crystalline penicillin, 50,000 units per cubic centimeter gave negative immediate and delayed reactions. Trichophyton test with rugose and praeformans were negative. All other tests were done.

**CASE 2**—A 43-year-old white woman had an infected sebaceous cyst in the left axillary region of one week's duration. She was given three daily injections, each of 200,000 units intramuscular in paracetamol and benzocaine. The signs of inflammation about the cyst subsided promptly. Eight days after the first injection of penicillin she noted tenderness of 101° F and tenderness of both buttocks. On the next day both buttocks were markedly swollen and tender and gave reaction to deep diathermy. In addition, there was circular area of erythema and edema of the skin with sharp raised edge quite typical of erysipelas. The central area of the skin lesions was faintly yellow. Under expectant treatment the fever subsided in three days. Simultaneously the lesions in both buttocks regressed, leaving residual areas of induration along the track of the original needle punctures. The latter resorbed in five weeks leaving both buttocks normal.

The only previous contact with penicillin was brief course of oral penicillin one year before at which time there had been no unusual reaction. The patient gave no personal history of allergy. One brother had both hay fever and ekema, her paternal grandfather had ekema, and her daughter had ekema in 6 months.

Skin tests with crystalline penicillin gave negative immediate and delayed reactions. Her skin penicillin protein test was negative. No common inhaled and pollen. Trichophyton test was positive.

**CASE 3**—A 16-year-old white woman complained of tender area over the tip of the coccyx of three days' duration. Over the buttock over the coccyx there was a pilonidal cyst as usual. The patient was in the left buttock. By the third day of treatment the pilonidal cyst was drained and drained. Nine days after the injection of penicillin the patient complained of pain in the left buttock. Examination

tion revealed moderate tenderness and swelling. The buttock is the region of the original needle puncture. Temperature was  $100^{\circ}\text{F}$ . The next day the temperature was  $102^{\circ}\text{F}$ . The buttock a markedly swollen and edematous tenderness was so great that pressure ambulation. The skin over the buttock showed an erysipeloid reaction precisely circular in shape with sharp raised border. In addition there were joint pains, rigors, and coryza. The fever persisted for three days. The tenderness and swelling of the buttocks subsided in two weeks leaving residual nodules infiltration along the needle track. These subsided in further three weeks. There was past history of mild upper respiratory symptoms during the spring grass season for the last three years. Unfortunately the patient was not available for skin test.

CASE 4—A 33-year-old man came had acute left valvular adenitis of four days duration. Glucocorticoids were given and tender but were not fluctuant. He was given 100,000 units of penicillin in saline solution at three-hour intervals followed by two daily injections of 200,000 units of penicillin in peanut oil and beeswax. The adenitis subsided in 10 days. Fever for the last injection of penicillin in oil and beeswax the patient noted small painful nodules at the sites of the injections. These lesions developed so that by the eighth day the skin over the buttock displayed erysipeloid lesions with sharp raised edge and cyanotic center. The buttocks had become intensely swollen and tender. The temperature  $103^{\circ}\text{F}$ . The next day the fever subsided somewhat but the patient later developed joint pain, coryza, rigors, and moderate to severe headache. The peak of this general reaction occurred while the severe local reaction was beginning to subside. From this time on, he remained locally recumbent, so that eighteen days after the last injection the skin was well except for small persistent nodules at the site of the injections. The latter subsided at the end of one month. In addition to symptomatic treatment the received frequent doses of epinephrine but the latter had no obvious effect on the lesion in the buttock. One month previously the patient had had three intramuscular injections of aqueous penicillin without reaction. Some days previously the patient had developed generalized eruptions several days after treatment with sulfadiazine. He had tendency to mild or moderate rigors after taking warm baths and several days before he had generalized rigors for several hours. Some days previously he had had mild local swelling as a result of his sting.

Skin tests with crystal line penicillin gave negative immediate and delayed reactions. Test with trichophyton are negative. Skin test protein 0.001 mg autogenous plasma test per cent extract negative. There are also positive reactions to ingested plasma, penicillin, and alkali.

#### DISCUSSION

The reactions described in this paper are probably common. Thus the four instances here reported have occurred in a series of fifty in which penicillin in peanut oil and beeswax has been administered. Other physicians have told us informally of frequent similar experiences. Despite this, only one instance of this kind appears to have been reported in the literature thus far. Although individual reactions following penicillin in peanut oil and beeswax have been mentioned by other writers, little attention appears to have been paid to these very intense delayed local responses. For example in a large series of patients treated with this preparation of penicillin Romanovsky<sup>2</sup> although noting local reactions does not give a description of the lesion, nor does he indicate that their appearance may be alarming.

The reaction we describe seems to be characteristic of the penicillin in oil and beeswax preparation and not of penicillin in saline solution. In a group of well over 1,000 patients receiving multiple intramuscular injections of penicillin in saline solution we have never seen a local reaction of this kind.

It is of practical clinical importance that the general physician and surgeon be aware of this type of localized allergic reaction to penicillin in oil and beeswax because it can be readily confused with an inflammatory lesion caused by infection. We have been informed of a trial cases in which fruitless attempts at incision and drainage were made, resulting only in prolonged illness. In another patient whom we encountered, the attending physician had prescribed additional penicillin in an effort to combat the supposed local infection. The significance of this reaction as an allergic manifestation and its completely benign prognosis thus deserve wider recognition.

The probable mechanism deserves some comment. It appears likely that these severe reactions are analogous to local serum sickness. The predominant response is a local one presumably because the slowly absorbed preparation retains antigen at the site for a prolonged period for local reaction. The absence of similar reactions to penicillin injected in saline solution indicates the importance of the menstruum in determining the character of the reaction. The more general symptoms indicative of the serum sickness-like response were present in two of the cases, and fever occurred in all. It is probable that in addition to its localizing action, the oil and wax increase the antigenicity of the penicillin as a true an immunologic adjuvant as has been described especially by Pienn and co-workers.

The exact antigen causing the allergic response to penicillin in peanut oil and beeswax is not identified by the present observations. Probably it is the penicillin itself. Thus, Gray reported on the lack of antigenicity of beeswax. He referred also to previous observers who gave multiple intramuscular injections of 5 per cent beeswax in peanut oil in repeated series without any subsequent local reaction being observed. Experience indicates that peanut oil itself rarely causes difficulty as is testified by the lack of reaction to *syngonium* in peanut oil, even when used in atopic individuals. In Case 3 we obtained a plus reaction to bee protein; this patient gave a history of intense local reaction to a bee sting some years before. However, the prolonged incubation period in this, as in the other cases, suggests a newly induced sensitivity. If the buttock inflammation were due to pre-existing sensitivity one would have anticipated its rapid development within a period of twenty-four to forty-eight hours rather than after an interval of one or more weeks.

It appears plain that neither the beeswax itself nor the peanut oil is the probable cause of these reactions. In contrast, penicillin, whether amorphous or crystalline, has been found to induce syndromes which resemble serum sickness and allergic reaction fairly readily. In most of the instances

may account for the experience of localized allergic reaction to penicillin in peanut oil and beeswax could be avoided by changing to another brand.

In our brief series one of the patients was definitely an atopic individual; two others had a strong family history of atopic illness. Although such a con-

stitutional predisposition is doubtless not necessary to the development of this type of acquired sensitivity. It is possible that atopic persons react more readily.

The clinical management of this form of reaction to penicillin in oil and beeswax merits a little more detailed discussion. In order to reduce the occurrence of such reactions it is wise to employ a preparation containing crystalline rather than amorphous penicillin whenever possible. If a brand containing amorphous penicillin has been used it may be possible to substitute another brand, preferably of crystalline penicillin, in the hope that the actual antigen may be avoided. However if the reaction has been a severe one and the need for further penicillin is not especially urgent it is probably best to stop penicillin therapy altogether. When the indication is urgent it is preferable to change to intramuscular crystalline penicillin in saline solution or to any of the preparations of procaine penicillin. This should be given in small doses at first and preferably injected into the deltoids. At the same time the patient can be given antihistamine drugs, epinephrine or ephedrine as symptomatic medication. Thus it may be possible to tide the patient over this difficult period. Increasing the penicillin dosage as it appears to be tolerated until full therapeutic level are obtained. It would be advisable to observe the patient carefully for evidence of more severe allergic reaction such as intense urticaria, generalized edema or erythema, or any indication of a motor collapse. Should any of these occur it would then be imperative to stop the drug at once.

In most instances of newly induced penicillin sensitivity the allergic state is transient and penicillin can be re-administered without difficulty sometimes after an interval of only a few weeks. However this is not always the case and it therefore follows that caution must be observed in re-administering penicillin to a patient who has a history of a severe local reaction to penicillin in oil and wax such as is described in this paper.

Though in three cases in this group in which penicillin skin tests were performed they were negative both on immediate reading and at the forty-eight hour observation, previous experience with other forms of induced penicillin allergy would suggest that in a larger series a small percentage would show a positive forty-eight hour test. This would be of value both diagnostically and as a guide to the persistence of sensitivity to penicillin. The presence of a positive test would indicate the need for even greater caution in administering the drug. Desensitization with penicillin could be tried and has been found effective in other forms of penicillin allergy.

#### SUMMARY

1. Four cases of severe delayed local reaction to penicillin in oil and beeswax are presented.
2. The reaction is of such intensity as to mimic bacterial infection with cellulitis and suppurations. Fever and malaise are usual accompaniments.
3. Although alarming in its initial appearance the reaction resolves completely without specific treatment.
4. The allergic nature of the reaction is indicated by the latent period of seven to ten days, and by associated symptoms of urticaria and joint pains.

It is of practical clinical importance that the general physician and surgeon be aware of this type of localized allergic reaction to penicillin in oil and beeswax, because it can be readily confused with an inflammatory lesion caused by infection. We have been informed of actual cases in which fruitless attempts at incision and drainage were made resulting only in prolonged illness. In another patient whom we encountered, the attending physician had prescribed additional penicillin in an effort to combat the supposed local infection. The significance of this reaction as an allergic manifestation and its completely benign prognosis thus deserve wider recognition.

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4. The allergic nature of the reaction is indicated by the latent period of seven to ten days, and by associated symptoms of urticaria and joint pains.

5. The results of skin tests with penicillin, peanut oil, and bee protein are discussed. Penicillin is considered the most probable antigenic factor the menstruum enhancing its antigenic activity.

6. Practical clinical management is presented.

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## ADVANCES IN ANESTHESIA

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ADVANCES in anesthesia follow several lines of endeavor. I shall try briefly to mention some of them. For example, the most notable situation in history exists today in the fact of the great latitude in choice of agents and methods. In nitrous oxide one has a mild, quick-acting analgesic agent associated with a short period of recovery and relative safety in respect to fire and explosion hazards. This agent is generally available and is used rather skillfully by a large number of individuals. Ethylene similarly is generally available and although the fire and explosion hazard which attends it has limited its use, it is still one of the outstanding agents from the standpoint of safety in the anesthetization of patient suffering from shock or heart disease. Cyclopropane is potent and is accorded widespread use. It is not free of hazard from fire and explosion but it is capable of producing better relaxation than are any of the other gases. The period of induction is short. The occasional difficulty encountered when an untoward result is observed just as the anesthesia has been terminated is not fully understood, but apparently it is peculiar to certain techniques of the administration of cyclopropane. I refer to the so-called cyclopropane shock that is seen at the termination of anesthesia in an occasional case.

The devices with which the gases are administered have not been improved for many years, and probably will not be until adequate mechanisms for the analysis of the atmospheres within the breathing bag and various parts of the machine are developed. I think that it is safe to say that this advance can be anticipated either this year or next year.

Of the several types of ether that have been developed, none seems to be better than diethyl ether. In this centenary year of the use of chloroform it is interesting to notice that anesthesia produced with this agent still is fraught with danger and that chloroform has certain qualities which make it an agent tempting to man and reports on its use from time to time are still given. It would seem that the safe or originally accorded chloroform might have been more prolonged had it not been for the introduction of so many good agents in the last few years. Another agent is ethyl chloride. Very few reports concerning this agent are seen now probably because, like chloroform, it is not generally used.

In the field of local anesthesia various agents have been introduced such as Eupercaine, Pontocaine and others. These agents seemed to be required because prolonged anesthesia could not be maintained with a single dose of procaine hydrochloride. This was especially true in block and pinal anesthesia. Lermontov's introduction of continuous pinal anesthesia was followed by Tuohy's modification of Lermontov's method which was in general an adaptation of Adams'

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5 The results of skin tests with penicillin, peanut oil, and bee protein are discussed. Penicillin is considered the most probable antigenic factor, the menstruum enhancing its antigenic activity.

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## ADVANCES IN ANESTHESIA

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ADVANCES in anesthesia follow several lines of endeavor. I shall try briefly to mention some of them. For example, the most notable situation in history exists today in the fact of the great latitude in choice of agents and methods. In nitrous oxide one has a mild, quick-acting analgesic agent associated with a short period of recovery and relative safety in respect to fire and explosion hazards. This agent is generally available and is used rather skillfully by a large number of individuals. Ethylene similarly is generally available, and although the fire and explosion hazard which attends it has limited its use, it is still one of the outstanding agents from the standpoint of safety in the anesthetization of patients suffering from shock or heart disease. Cyclopropane is potent and is accorded widespread use. It is not free of hazard from fire and explosion, but it is capable of producing better relaxation than are any of the other gases. The period of induction is short. The occasional difficulty encountered when an untoward result is observed just as the anesthesia has been terminated is not fully understood, but apparently it is peculiar to certain techniques of the administration of cyclopropane. I refer to the so-called cyclopropane shock that is seen at the termination of anesthesia in an occasional case.

The devices with which the gases are administered have not been improved for many years, and probably will not be until adequate mechanisms for the analysis of the atmospheres within the breathing bag and various parts of the machine are developed. I think that it is safe to say that this advance can be anticipated either this year or next year.

Of the several types of ether that have been developed, none seems to be better than diethyl ether. In this centenary year of the use of chloroform it is interesting to notice that anesthesia produced with this agent still is fraught with danger, and yet chloroform has certain qualities which make it an agent tempting to many, and reports on its use from time to time are still given. It would seem that the factor originally accorded chloroform might have been more prolonged had it not been for the introduction of so many good agents in the last few years. Another agent is ethyl chloride. Very few reports concerning this agent are seen now, probably because like chloroform it is not generally used.

In the field of local anesthesia various agents have been introduced such as Nupercaine, Pontocaine and others. These agents seemed to be required because prolonged anesthesia could not be maintained with a single dose of procaine hydrochloride. This was especially true in block and spinal anesthesia. Lemon's introduction of continuous spinal anesthesia was followed by Tuohy's modification of Lemon's method which was in general an adaptation of Adams.

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5 The results of skin tests with penicillin, peanut oil, and bee protein are discussed. Penicillin is considered the most probable antigenic factor the menstruum enhancing its antigenic activity

6 Practical clinical management is presented.

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that sodium has been administered within a few minutes without the production of satisfactory anesthesia, then an additional dose of morphine could be injected intravenously. This additional dose usually should be  $\frac{1}{4}$  to  $\frac{1}{2}$  gr (0.008 to 0.01 Gm.)

Nevertheless, it is realized that Pentothal sodium does not provide everything that might be desired in an intravenous anesthetic agent. Therefore, further investigations have been made for new agents, or suggestions have been advanced that something might be combined with Pentothal sodium to give it the potency which it lacks.

The question of relaxation of the patient is of prime importance to both surgeon and anesthesiologist. The advent then, of curare in medical practice especially in connection with the administration of anesthetic agents, has made a great impression on those who have used it. Curare produces excellent relaxation, with relatively little postoperative prostration. It has been used most commonly in association with cyclopropane anesthesia in which relatively large quantities of oxygen are used. Curare and cyclopropane especially when an intratracheal tube is used to administer the anesthetic agent give a result that is highly desirable in most instances. The great impression caused by this particular combination stimulated the use of curare with nitrous oxide ethylene and also other anesthetic agents. In the latter instance less curare is required than when curare is used with the gases. The use of curare with Pentothal sodium has been tried repeatedly in which a combination curare does give a degree of relaxation that Pentothal sodium in itself cannot provide. Recently Baird suggested the use of Pentothal sodium plus curare the curare preferably having the form of a solution of d-tubocurarine chloride. Baird was greatly impressed with the results of administration of these agents in combination in one syringe, the mixture being 0.5 mg. of d-tubocurarine chloride per cubic centimeter of 2.5 per cent solution of Pentothal sodium. At the same time oxygen or nitrous oxide and oxygen administered to keep the patient oxygenated.

In this respect we ought not to forget that the anesthesiologist's understanding and actual use of stimulants and supportive measures are hardly less important than the method of anesthesia employed, whatever it may be. This is a consideration of the utmost significance which serves to emphasize the need for extension of the period of the anesthesiologist's training to which I shall advert later.

As we look back and examine the present and speculate as to the future, it would appear that the status of anesthesia now is relatively good and that apparently it will improve. This opinion is based strictly on the agents available now and on those which it is possible to envisage. An additional important phase however of the present status of anesthesia is that more and more physicians have interested themselves in the field of anesthesiology. A number of institutions have established either temporary or fully approved residencies in this specialty and in some instances prominent anesthesiologists may teach by the preceptor method. The board for proficiency in the Association, all actively de-



technique for the production of continuous caudal anesthesia. That is, by use of a catheter instead of a needle it became possible to produce anesthesia of desired length with procaine hydrochloride. This was important because I believe procaine hydrochloride is the safest available agent for local anesthesia. Here is an instance in which improvement in technique has greatly increased the efficiency of an old agent and it is an outstanding advance in anesthesia whenever that result can be obtained.

The introduction of the Magill intratracheal tube was without doubt a great advance in inhalation anesthesia. This technique is used extensively to great advantage now in many types of surgery. For intracranial operations it has made the patient's breathing quiet and has obviated the increased intracranial pressure which often occurred when an anesthetic agent such as ether was administered for this sort of operation. Use of the intratracheal tube in plastic surgery is essential so that the surgeon may have the operative field to himself and so that it may be kept sterile. One of the most important applications of the intratracheal tube is in thoracic surgery where it permits the lungs to be inflated at will during the operation with the thorax opened. In abdominal surgery the quietness of respiration which the technique ensures is desirable, and the ease with which the anesthetic agent can be introduced into the lungs and from there into the blood stream and thence to the nervous system has increased the efficiency of inhalation anesthesia generally. The Magill technique is especially valuable when an operation is to be performed on a patient's back and he must be placed in the prone position. In all the operations mentioned, and with all the various anesthetic agents suited to the technique it is possible with the tube in place, to aspirate material from the trachea and bronchial tree both during anesthesia and for a short period afterward. This decreases morbidity and mortality rates considerably.

Intravenous anesthesia gradually has won widespread favor largely because of Pentothal sodium. It is generally recognized that administration of this agent should be preceded by preliminary medication, usually with a barbiturate and morphine and atropine. The dose of Pentothal sodium should be kept relatively small; that is, usually it should not be more than 1 or 2 Gm. for a patient. It is definitely understood that solutions of Pentothal sodium stronger than 5 per cent are hazardous. In combining nitrous oxide and oxygen (50 per cent of each) and using this mixture in association with Pentothal sodium, we are able definitely to reduce the amount of Pentothal sodium that otherwise would be administered. The administration of small quantities of Pentothal sodium to induce anesthesia before inhalation anesthesia is begun has been much appreciated by patient. The technical point of importance in this connection is that not more than 10 cc. of a 5 per cent solution of Pentothal sodium should be administered before inhalation anesthesia is begun and it is better if the amount can be kept to 6 or 7 cc. Larger amounts of Pentothal sodium interfere with the depth of respiration, and therefore interfere with production of the desired result with the inhalation anesthetic agent. A second technical point in the use of Pentothal sodium is that if the effect of the preliminary medication on the patient is minimal and if when 10 or 15 cc. of 5 per cent solution of Pento-

# THE APPLICATION OF MYOTOMY TO TENDON REPAIR IN THE FINGERS

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(From the Hand Service of the Bellevue Hospital)

SEVERAL years ago myotomy was introduced as a maneuver facilitating the repair of divided flexor tendons of the hand. With growing experience it soon became apparent that this procedure possessed several virtues. It not only makes easier the handling of the divided tendon ends by eliminating the usual tension but obviates the danger of disruption of the suture line, as well. Finer suture material can be used and early active motion is permissible.

This presentation is particularly concerned with the application of myotomy to tendon laceration in the proximal and middle phalanges of the fingers. This is the area where the worst results are to be expected. Bunnell has discussed the reasons for this and has described his method of handling the problem. With the aid of myotomy it is possible to treat the situation somewhat differently to attain the objective.

The incision described by Bunnell is used. It runs from the web to just beyond the distal flexor crease on the lateral surface of the finger midway between the volar and dorsal aspect. The incision is planned directed posterior to the solar distal nerve and vessel and exposes the entire extent of the digital flexor sheath, regardless of the location of the wound. The proximal tendon end is sought for and seized with an artery forceps. Every effort is naturally made to disturb the sheath as little as possible. A linear incision is then made just above the wrist and the corresponding muscle belly identified as shown in Fig. 1. Where the ulnar tendon is also cut it is exposed, only the profundus being paired. A small part of the proximal portion of the ulnar tendon is cut away as can and be delivered into the wound.

Following the myotomy the proximal profundus tendon end is then pulled down toward the point of tendon insertion at the base of the distal phalanx. If the degree of retraction allows it to reach all the way the entire distal tendon end is resected and the proximal end is then sutured as shown in Fig. 2 to the base of the distal phalanx and the attached stump of tendon insertion. Where it is not possible to bring the proximal end thus the ends of the distal tendon is resected so that the suture sits somewhere in the middle phalanx at a point distal to the location of the wound. A cuff of sheath is preserved on the middle phalanx through which the tendon is passed.

The finger can be jointed postoperatively in extension with slight flexion at the wrist. The advantage of avoiding a bulky tendon suture at the site of injury of the sheath, surrounding tissues, and skin is obvious.

The indications for immediate tendon repair have remained the same in principle on this Hand Service as at the time of their original adoption in 1933 following the publication of the article of Koeh and Mason. In two of the

for skilled physician anesthesiologists exceeds the supply and no doubt will continue to do so for some time but the opportunities for training have been expanding so rapidly and are being so carefully scrutinized from time to time that I cannot say that the outlook as to supply is at all hopeless. As a matter of fact, the opportunities for physicians in this field are great and will continue to become greater. The inclination now is for a physician anesthesiologist to meet only the minimal requirement of two years of training, but eventually I think such training will entail three years.

World War II substantiated the prophecy that anesthesia would become much more important after the war than it was before. It seems conservative to say that anesthesia has gained great momentum and an important position in the United States, Canada, and the British Isles, and that it is also gaining considerable momentum in most other modern countries throughout the world. As I have said, the present status of anesthesia may be considered to be excellent, in so far as the beginning of the second century of its use is concerned, especially when we realize that much of the progress was made in the first few years and the last few years of the first century of its use.

O. O. T. (Admission 45410) 21 yr. old fireman, was admitted on Jan. 7, 1947 shortly after cutting the middle phalanx of the left middle finger on broken glass. He suffered division of the flexor profundus tendon and of the volar digital nerve on the radial side. Following the usual technique an incision was performed which allowed the suture of the profundus tendon and met the normal insertion of the tendon at the base of the terminal phalanx. Neurotomy was simultaneously performed. This patient was able to flex his finger completely within four months. Function as normal.

M. M. (Admission 45487) 4 year old clerk had originally suffered laceration on the volar aspect of the middle phalanx of the right index finger on Feb. 3, 1947. The wound was dirty for which reason only the skin was sutured and an infection ultimately developed with pus formation. In April 3, 1947 repair of the divided flexor profundus tendon had been recognized being present after surgery. Devised for. Following the usual technique the profundus tendon was found and directed free from somewhat dense adhesions. Following incision it was possible to perform tenorrhaphy near the tendon insertion. The usual plaster immobilization of the entire hand then followed after 48 hours of therapy began. The patient regained complete function of the finger within four months.

#### SUMMARY

Three cases in which myotomy has been performed to facilitate the repair of flexor tendons divided in the fingers are presented.

The procedure of myotomy is a simple technical expedient that makes possible the easier handling of these cases and allows the attainment of certain desirable objectives in this type of surgery.

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three illustrative cases presented in detail the requirements for immediate tenorraphy were satisfied. It may be parenthetically added that the advent of penicillin has not altered our insistence on a reasonably clean wound in addition to other factors before proceeding with operative treatment in the fresh case.

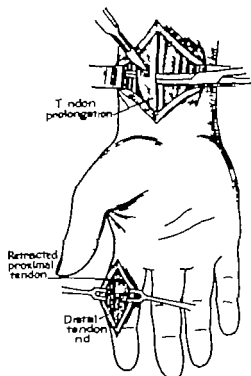


Fig. 1

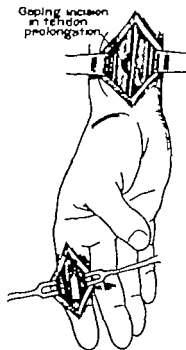


Fig. 2

—passed the proximal  
has been delivered

line has the  
The proximal end  
of tendon has been

#### CASE REPORTS

T. B. (Admission 47637) 50 year old house fr. was admitted Sept. 8 1946, shortly after cutting the right ring and little fingers while preparing lunch. She suffered to distal lacerations of the volar aspects of both fingers at the proximal interphalangeal joints. Examination revealed evidence of division of both flexor tendons to the little finger as well as of the ulnar ulnar digital nerve to the finger. In the ring finger the flexor profundus tendon had been divided. Under general anesthesia and with the aid of an Esmarch bandage, profundus tenorrhaphy and neuroorrhaphy were performed. Myotomy was successfully used. In both fingers the distal tendon ends were exposed down toward their location so that the tenorrhaphy site was located near the insertion in the terminal phalanx. All suture from the wounds in the sheath and integument. A posterior moulded plaster splint was then applied and left on for the first five days. This patient improved progressively but when last seen several months after operation still showed some defect in complete flexion in both fingers.

atisfy all requirements is borne out by the almost universal suspicion of multiple neoplasia of certain systems, such as skin of paired organs such as breast and ovaries, as well as stomach and colon. Also in question are some of the more complex type of growths such as carcinosarcoma lymphosarcoma multiple myelomas, and similar lesions noted for multiplicity. In the more critical surveys many of such types of cases have been excluded.

The incidence of multiple malignant neoplasms has been variously reported from 0.9 per cent to 8 per cent of all malignant cases. Hanlon reported 18 cases of multiple primary malignancy in 960 cases of malignant tumors, or 1.9 per cent. Warren and Gates, in 1931, were the first to make a critical survey of the literature. They reported 40 cases in 1,078 cancer autopsies, or 3.7 per cent, and in addition analyzed 1-19 cases of multiple primary malignancy collected from the literature. For the entire 1-19 cases the incidence was found to be 1.8 per cent when American and European data were combined and 3.9 per cent for American data alone. Hurt and Broders reported 71 cases of multiple primary malignancy in 1,144 cancer cases, or 3.3 per cent. Lund found 84 multiple cases in 1,416 cases of cancer of the mouth 31 of which were multiple cancer of the buccal mucosa alone or 6 per cent. Bugher<sup>1</sup> found 30 cases in 983 cancer autopsies or 3.1 per cent. In this same paper after working out an editorial statistical analysis he concluded that the actual incidence of multiple primary malignancies exceeded the expected incidence on the basis of chance alone and that there is an inherited susceptibility to cancer possessed by a portion of the population. This idea is supported by most authors. Nehrelner and White<sup>2</sup> found 37 multiple cases in 11,211 cancer cases, or .7 per cent. Burke<sup>3</sup> reported an incidence of .8 per cent with 46 multiple cases in 5,833 cancer autopsies. Austin<sup>4</sup> reported 86 cancer autopsies with .7 per cent of multiple cancers. Kutschbaum and Shively<sup>5</sup> found 1 per cent in 1,411 cancer autopsies and Deane<sup>6</sup> reported 3,115 cancer cases, eliminating all cases of multiple tumors of the same system finding 36 cases of multiple growths, or 1 per cent. He also cited Regaud<sup>7</sup> as reporting the lowest incidence .0.9 per cent, with only 9 multiple malignant cases in 1,099 surgical cases of cancer. Stalker and co-workers<sup>8</sup> reported 113 cases of multiple growths in 2,500 surgical cases of cancer or 4.5 per cent. Gaudin<sup>9</sup> reported 3.6 per cent of multiple growths in 4,610 cancer patients on whom follow up studies were carried out for 40 years. Peller<sup>10</sup> found 270 multiple cases, 4.6 per cent in 5,876 cancer cases and believed that the actual rate of multiple malignant growth was less than the expected rate. Phillips<sup>11</sup> reported multiple skin cancers may vary from 0 to 30 per cent per patient with an average incidence of 16.0 per cent. This substantiates the findings of almost all authors that the highest incidence of multiple malignant growths occurs in the skin. It is also of interest in this respect that Gaudin<sup>9</sup> has pointed out that 70.0 per cent of all patients with skin cancers had more than one primary malignant growth. Tullis found 0 per cent of multiple malignancies in 1,044 cancer autopsies. Hellendall<sup>12</sup> found 4.3 per cent in 679 cancer autopsies.

Of all publications on this subject the recent work of Warren and Ehrenkrantz<sup>13</sup> represent the most extensive and thorough investigation for it includes

## MULTIPLE PRIMARY CARCINOMA

FRANCIS T. H'DOUBLET, M.D. AND A. DENTON VAIL, M.D. SPRINGFIELD, Mo

SINCE 1869 when Billroth reported the first two cases of multiple primary malignancy a gradually increasing interest in the subject has been aroused. Through the succeeding years much data have accumulated on the subject until at this time the condition which was once considered a rare phenomenon, is recognized as being fairly common and the reporting of sporadic cases is hardly justified unless the material will be a definite contribution.

In view of the manifold and bizarre nature of malignant growths, it was immediately necessary to set up criteria the fulfillment of which were intended to establish the independency of the various lesions, and the following were Billroth's postulates: (1) Each tumor must have an independent histologic appearance; (2) the tumors must arise in different locations; and (3) each tumor must produce its own metastases. A few years later Mercanton advocated the addition of a fourth postulate: That the patient remain free from the disease following operation thereby demonstrating that the growths were separate entities and were not themselves metastases. In light of present knowledge of cancer it is obvious that in the interests of critical evaluation these criteria cannot be rigidly adhered to. A Scofield<sup>1</sup> has pointed out, metastases and recurrences frequently show marked cell change from original cell type. Conversely multiple malignant growths occurring in systems or paired organs may readily be primary growths although exhibiting like histologic pictures. Because of change in cell type during metastasis it may be possible to confuse such growths concluding it to be the primary focus and again, because of these changes in cell type it may not be possible to prove that an apparently primary growth is not a metastasis. These facts, together with the knowledge that malignant tumors may exist without metastases, are evidences of the weakness in these postulates. Kretschmer<sup>2</sup> also referred to the difficulty in meeting the third postulate in that the patient may and preferably does, come early in the course of the disease, long before metastases have had time to develop. He also points out that metastases may be so small as not to be demonstrable clinically. Goetze<sup>3</sup> advocated a revision of these criteria as follows: (1) The tumors must have the macroscopic and microscopic appearance of the usual tumors of the organ involved; (2) exclusion of the probability of one tumor being the metastasis must be certain; and (3) the diagnosis may be confirmed by the character of the individual metastases. While the authors of several excellent papers, notably Hanson, Hurt and Broders,<sup>4</sup> and Stalker and associates,<sup>5</sup> have followed these postulates, there remains the possibility of error due to the fact that in the diagnosis of multiple malignancy the exclusion of the possibility of one neoplasm being a metastasis may pose a most difficult problem. Realizing this, Warren and Gates<sup>6</sup> have set up the following criteria which have now gained general acceptance: (1) Each of the tumors must present a definite picture of malignancy; (2) each must be distinct; and (3) the probability of one being the metastasis of the other must be excluded. That this does not completely

satisfy all requirements is borne out by the almost universal suspicion of multiple neoplasms of certain systems, such as skin of paired organ such as breast and ovaries, as well as stomach and colon. Also in question are some of the more complex type of growths such as carcinosarcoma, lymphosarcoma, multiple myelomas, and annular lesion noted for multiplicity. In the more critical surveys many of such types of cases have been excluded.

The incidence of multiple malignant neoplasms has been variously reported from 0.9 per cent to 1.8 per cent of all malignant cases. Hannon reported 18 cases of multiple primary malignancy in 900 cases of malignant tumors, or 9.5 per cent. Warren and Gates, in 1935, were the first to make a critical survey of the literature. They reported 40 cases in 1076 cancer autopsies, or 3.7 per cent, and in addition analyzed 1,119 cases of multiple primary malignancy collected from the literature. For the entire 1,193 cases the incidence was found to be 1.8 per cent when American and European data were combined and 3.9 per cent for American data alone. Hunt and Broders reported 71 cases of multiple primary malignancies in 2,144 cancer cases, or 3.3 per cent. Lund found 94 multiple cases in 1,448 cases of cancer of the mouth, 31 of which were multiple cancer of the buccal mucosa alone, or 6 per cent. Bucher<sup>1</sup> found 30 cases in 683 cancer autopsies, or 4.4 per cent. In this same paper after working out an elaborate statistical analysis he concluded that the actual incidence of multiple primary malignancy exceeds the expected incidence on the basis of chance alone and that there is an inherent susceptibility to cancer possessed by a portion of the population. This idea is supported by most authors. Selbreiner and Weber<sup>2</sup> found 307 multiple cases in 11,111 cancer cases, or 2.76 per cent. Burke<sup>3</sup> reported an incidence of 7.4 per cent with 46 multiple cases in 623 cancer autopsies. Austin reported 647 cancer autopsies with 7 per cent of multiple cancers. Kirschbaum and Shilev<sup>4</sup> found 1.1 per cent in 1,411 cancer autopsies and Desai<sup>5</sup> reported 3,115 cancer cases, eliminating all cases of multiple tumors of the same stem finding 36 cases of multiple growths or 1.16 per cent. He also cited Regnaud<sup>6</sup> reporting the lowest incidence, 0.5 per cent with only 9 multiple malignancies in 1,099 surgical cases of cancer. Stalke and co-workers<sup>7</sup> reported 113 cases of multiple growths in 1,000 surgical cases of cancer, or 11.3 per cent. Claudon<sup>8</sup> reported 1.6 per cent of multiple growths in 4,617 cancer patients in whom follow-up studies were carried out for 40 years. Peller<sup>9</sup> found 70 multiple cases, 4.6 per cent in 5,876 cancer cases and believed that the actual rate for multiple malignant growths was less than the expected rate. Phillips<sup>10</sup> reported multiple skin cancers may vary from 0 to 30 per cent per patient with an average incidence of 16.0 per cent. This substantiates the findings of almost all authors that the highest incidence of multiple malignant growths occurs in the skin. It is also of interest in this respect that Claudon<sup>8</sup> has pointed out that 20.0 per cent of all patients with skin cancers had more than one primary malignant growth. Tull<sup>11</sup> found 9.0 per cent of multiple malignancies in 1,044 cancer autopsies. Hellsdall<sup>12</sup> found 4.3 per cent in 618 cancer autopsies.

Of all publications on this subject the recent work of Warren and Fhrenreich<sup>13</sup> represents the most extensive and thorough investigation for it includes



the study of 184 additional cases of multiple malignancies which, combined with the data from the previous report of Warren and Gates,<sup>1</sup> represents a study of 1453 cases of multiple primary malignancy. Of these cases, 234 cases represent their own material, secured from 3,907 cancer autopsies, or an incidence of 6.0 per cent. Other significant data brought out by this wide experience may be mentioned: the average age for males with multiple malignancy was 65.1 years, for females 56.9 years; sex ratio showed a preponderance of males, 1.1 autopsies revealed a higher incidence of multiplicity in males, whereas surgical experience gave a higher incidence in females. A study of the distribution, by site, of the lesions showed that the large intestine was involved in 3.6 per cent, prostatic in 26.8 per cent, skin 17.5 per cent, pharynx 18.0 per cent, stomach 13.9 per cent, breast 12.9 per cent, uterus 11.3 per cent, with miscellaneous organs accounting for the remainder. They concluded that there is no constant ratio between organs involved in series of one cancer and in series of two or more cancers, with the exception of the large bowel. Study of the survival rates indicated that multiple malignant growths in themselves did not alter the survival rate to any appreciable degree. From their data, they believed that the presence of numerous malignant tumors did not necessarily imply a worse prognosis.

The literature contains few publications of cases presenting three or more primary malignancies in the same individual since the condition is extremely rare. Warren and Gates found only three cases. McNamara, Kulikowska and Hoerner, Davis and Hanelin, Nemours-Auguste<sup>20</sup> and Portuondo<sup>21</sup> reported only 1 each and in all of these the third tumor was found only at autopsy. Warren and Ehrenreich<sup>22</sup> reported 1 case. Drooker<sup>23</sup> determined that in general, triple malignancies of miscellaneous organs comprise 2.9 per cent of all cases of multiple malignancy. Couvillor and Butsch<sup>24</sup> stated that multiple malignant tumors of the same organ are much more rare than the incidence in different organs.

Almost equally limited in number are those cases of multiple primary malignancy in which the thyroid gland is involved. In triple malignancies where two of the primary tumors originate in the thyroid, it is possible that only one case other than that reported here, has appeared in the literature. Galtikow<sup>25</sup> reported 1 case of adenocarcinoma of the breast and carcinoma of the thyroid. Wenker<sup>26</sup> was reported by Neprjachin as having had a case of carcinoma of the thyroid with carcinoma of the uterus. Tschirg<sup>27</sup> reported 1 case of carcinoma of the prostate with osteochondrosarcoma of the thyroid. Hannon<sup>28</sup> series contained 4 cases: adenocarcinoma of the thyroid (this is listed as adenocarcinomas so that it is possible that in this case there were multiple primary growths in the thyroid) and sclerous carcinoma of the breast, papillary carcinoma of the ovary and adenocarcinoma of the thyroid, adenocarcinoma of the thyroid and adenocarcinoma of the kidney, and adenocarcinoma of the thyroid with adenocarcinoma of the colon. Hornum and Schabed<sup>29</sup> reported 1 case of carcinoma of the thyroid and carcinoma of the uterus. Hurt and Broder<sup>30</sup> had 1 case of adenocarcinoma of the thyroid with lymphosarcoma of the groin. Schreiner and Weber<sup>31</sup> had 1 case with carcinoma of the thyroid and carcinoma of the breast. Stalker<sup>32</sup> listed cases in which the thyroid was one of the organs involved but other details were not given. Markowitz and Huerta<sup>33</sup> reported 1

case of adenocarcinoma of the thyroid, bilateral embryonal cell carcinoma of the ovaries, and carcinoma simplex of the breast. White<sup>21</sup> had one case of adenocarcinoma of the thyroid with squamous-cell epithelioma of the lip. Warren and Ebreneich<sup>22</sup> reported 4 cases. 2 were adenocarcinomas and 2 were carcinoma simplex of the thyroid with the other organs involved being uterus, esophagus, breast, and prostate.

### CASE HISTORY

Mrs J. H. Only the pertinent findings are given. The chief complaint was goiter. A enlargement in the neck had been noted first twenty-five years previously. Several attacks of choking had occurred at various intervals. The last attack occurred within a short interval. The enlargement then subsided but not as yet when it again slowly started to grow and continued to increase in size. In the year preceding admission there was troublesome choking and strangling when drinking liquids. Nervousness started five years before and increased. She was easily excited, cried easily, became blue and depressed, and worried great deal in the past year. She tired easily and there was increased difficulty sleeping. One of her people made her nervous. In the past six months had noticed increased irritability from sources usually considered significant. There had been enlargement of the knees on going upstairs. The patient had always slept with feet out of the covers but heat intolerance had increased in the past few months. Shortness of breath was present during past few months and was produced by moderate activities which had before not bothered her. Mild exertion caused the heart to beat faster than usual. She felt tired and worn out in the mornings. Appetite had always been good but had decreased had been noted in the past six months. There was gain of ten pounds in the past six months. She had to clear her throat frequently and was bothered by slight hoarseness. A friend, whom she had not seen for number of years, noted a decided change in her on meeting. There was no cough.

History of past illnesses revealed an operation in 1933 for removal of tumor of the womb (This was probably polyp). Following this, for several months, she was bothered by fluttering of the heart. Five years before admission she was diagnosed as having thyroidectomy and was placed on iodine medication in preparation. She did not come to surgery and noted no improvement in the condition from the medication. For the past year she had no dyspnea. A period last year from two to three weeks. This was controlled by suction from the local physician.

Family history was of significance only in that there was no history of cancer.

Physical examination showed the forehead wrinkled poorly looking up. There was visible and palpable enlargement of the isthmus of the thyroid gland which was ordinarily on palpation and swallowing. It was firm but not hard and resistant to manipulation. The breast enlargement was movable mass in the right breast at about 12 o'clock which was about 4 inches diameter. This mass was discrete but not encapsulated. It was not attached and was freely movable. There were no palpable nodes in the axillary groups. The blood pressure was 170/70 and the rate 84. There was slight tremor of the outstretched fingers. There were many skin tumors on the face and back several of which were pigmented. The skin of the entire body showed the usual amount of skin with intensification on the neck and back where there was dermatographia. Reflexes and sensation of the degree were present.

Laboratory examination revealed red blood cell count of 4,410,000 hemoglobin 70 per cent white blood cell count of 14,000 differential polymorphonuclears 80 per cent, 1 lymphocyte 2 per cent monocytes 2 per cent eosinophiles 1 per cent small, one specific gravity 1.023, ambo acid reaction, faint trace of albumin, ratio of serum to

The right lobe was larger than the left and contained discrete nodules (Fig 1) measuring about 1 inch in diameter arising from the antero-medial surface near the lower pole and overriding the isthmus. The isthmus was also found to contain discrete nodules (Fig 2) measuring about three-fourths of 1 inch diameter located at its junction with the left lobe of the thyroid. Both lobes, isthmus, and pyramidal lobe were removed leaving a small stump on both sides, each of which measured about 1 inch by  $\frac{1}{2}$  inch. A small nodule of tissue inferior to the left lower pole was removed and proved to be thymus.

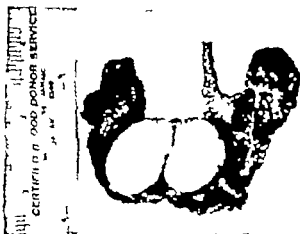


Fig 1.—The gross specimen with pyramidal lobe, showing section of larger tumor located in lower right lobe.



Fig 2.—Photomicrograph of larger tumor (Fig 1) showing cellular arrangement of cells early malignant change.

Pathologic report described gross specimens consisting of both lobes of the thyroid, isthmus, and pyramidal lobe, weight 30 grams. The main thyroid tumor presented nothing unusual. In the lower right lobe there was a nodule each on section was round, pinkish white, well encapsulated, and measured 2 cm in diameter. There was an identical nodule at the junction of the isthmus and the lower left lobe each measured 1.3 cm. in diameter. Microscopic examination of sections of the nodules from the right lobe (Fig 2) showed combination fibrous and pseudopapillary. There was no cellular infiltration of the capsule. Constituents of the tumor are of rather homogeneous cell structure. There was no

definite rim formation. The cells also had large vacuolated type of nucleus with faintly staining nucleolus. The nucleus was surrounded by moderate amount of eosinophilic protoplasm which was finely granular. Occasional eosinophiles were seen. Only an occasional mitotic figure was observed. The general picture showed a tendency to cordlike arrangement of the cells. There were some areas filled with hyaline-like material. In one area some small, well formed acini were seen. Some areas showed definite strandlike arrangement of the cell clusters with small well formed acini strands. Only small amount of connective tissue stroma was present.

Section of the smaller nodule (Fig 4) showed dense innervation capsule and a pseudocapsule. There was no cellular infiltration of the capsule. The cellular structure of this tumor was magnified picture of the previously described nodule. Here the nucleus

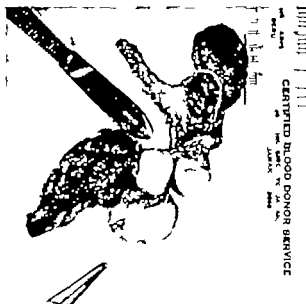


Fig 3—Thyroid gland showing section of smaller tumor located at junction of lobes with line to left lobe beneath points to larger tumor as seen in Fig 2.

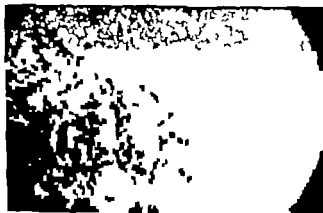


Fig 4—Photomicrograph of smaller tumor (Fig 3) malignancy of high grade.

of the cell as markedly hypochromat, large nucleated, and showed 1 to 2 nuclei. There was marked pleomorphism and there were many multinucleated cells. There was moderate amount of cytoplasm which was brownish with finely granular appearance. There was an occasional suggestion of anucleation.

Note: These tumors appeared to be separate entities, probably both arising from separate fetal denomas.

Diagnosis was double dermocarcoma of the thyroid, one showing well advanced, the other early malignant change.

Following an uneventful recovery from the roentgenomy the patient was returned to surgery April 12, 1945, at which time radical right mastectomy was performed.

Operative record listed radical right mastectomy with dissection of axillary fat which contained a number of small soft pink lymph nodes.

Pathologic report was scirrhus carcinoma of the breast grade 4 (Fig. 8).



Fig. 8.—Photomicrograph of breast tumor carcinoma, grade 4.

Again following uneventful recovery the patient was discharged from the hospital April 17, 1945. She was then given radiation therapy receiving 1,200 r to the thyroid area and 1,400 r each of the three breast areas. This was submitted to with some reluctance as she felt that the operation should have been sufficient. We have been advised by the local referring physicians that the patient died about a month later of generalized metastases. It is regrettable that we are unable to make additional studies on this case through the use of roentgen sections in an effort to identify the recurrent growth. Since biopsy attempts were not performed at that time we are unable to state the nature of the growth responsible for the terminal illness.

#### SUMMARY

1. Criteria for the establishment of independent malignancy of multiple origin are outlined with discussion of limitations.

— Incidence of multiple malignant neoplasms, as reported in the various studies in the literature is given.

3. Other statistics, as determined by previous surveys, are reported.

4. Triple primary malignancy is extremely rare. The limited number of these previously reported are cited.

5. One case of triple primary malignancy in which two of the primary growths originated in the thyroid, is reported here. Double primary malignancy of the thyroid gland is most unusual.



## DUPLICATION OF THE ENTIRE COLON AND LOWER ILEUM, WITH TERMINATION OF ONE COLON INTO A VAGINAL ANUS

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**D**UPLICATION of the entire colon appears to be a very rare anomaly. Weber and Dixon, in reporting their patient, a woman aged 47 years, reviewed the literature and were able to find only six previously recorded instances (1900 to 1945). In one of these (Gray) there was triplication of the colon. The patient an infant lived nine months and the situation was discovered at necropsy. Because of the rarity of this condition, the following case history is recorded and includes an account of the manner in which the anomaly was dealt with surgically.

### CASE REPORT

C. A. W. female aged 7 years, as admitted Sept. 29, 1947. In 1945 she had an ileal intussusception and was operated upon another hospital where an ileocecal tumor was found but not excised. Disproven. The tumor appeared to be situated in the low right abdomen and led to the posterior right pelvic wall. The intussusception was closed, after exploratory clinical diagnosis of carcinoma made, and no therapy administered. A vaginal anus had been noted prior to operation.

Because of the suspected ileocecal tumor the patient was referred to the Memorial Hospital for further management. Upon admission physical examination was essentially negative except for constant soiling of the clothing by feces, and the presence of a small anus on the posterior vaginal wall just within the vaginal orifice in addition to the normally placed one. When probed it did not lead to the common anal colon but the normal anus, but seemed to lead to a low lumen that was separated from the normal anal colon by partition. Examination of the abdomen was otherwise normal except for lower right rectus abdominis tenderness. There were no palpable masses. The x-ray was otherwise negative. Roentgenograms also showed anomalous development of the first and second ribs on both sides with striking syndactylism and pectoral thoracic asymmetry.

Later and anaesthesia urethral catheter as passed upward through the vaginal anus and it was found that this led into a low lumen which was separate from the normally placed anal colon. Further studies were tried out in vacuum of contrast media and the presence of the complete distal rectal colon was demonstrated (Figs 1 and 2).

A laparotomy was performed to the purpose of suppressing the function of the colon by the vaginal anus in order that it should be passed in the normal route.

The abdomen was entered through a low midline incision. Inspection and palpation of the pelvis revealed what apparently was a normal uterus, tubes, and ovaries. The pelvic and descending colon were duplicated and loosely applied (Fig 3). Blood vessels were present in the spaces between the two bowels. The latter were thickened and devoid of innervation and texture they appeared similar to what could have been hyperplastic segments of small bowel. In the region of the splenic flexure innervation and

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Weber, H. M. and Dixon, Claude F. Duplication of the Entire Large Intestine (Colon  
Duplex) Radiology 52: 218, 1946.

teous muscular ppe red & d ext aded proximally. The t anu re colon ppeared as single bow l (Fig 3) but th septum was visible through th Dd & d g the lumen in t. In th lower secnd g colon the bow l ga became separated leading t two cees with tw appendices, & ceum with t en appendices. For d st see t pprox mally ten inches bow the cees th re were t separat dion th t fast g int one proximally. N Meck l's d rctumum wa p present (Fig 4 d and B).

The remainder f the bicolonal recta ppeared normal.

The ta ppendices are excised.



Fig 1

Fig 1.—Barium enema fluoroscopy showing P/P both pelvic colons. H/H both hepatic flexures. 4/4 both ascending colons and A both sigmoides.



Fig 2

Fig 2.—Barium enema fluoroscopy showing P/T double transverse colons and D/D both descending colons.

A rubber covered bowel lamp was placed over the mid-descending colon and the pper sigmoid area p lkl incision were made through the bow l all t th lumen for dist one f foot 4 cm. The per anal gap f the wound were secured together with continuous csg sut re (f hecatan); and the rem side f the ne incision wa completed with t re f re t ssg tgnat sut. About 10 below the incision the medial one f the colons was p l l aded. The upper one l was closed by continuous ssgat sut re t h g l h ers. The lower wound treated in similar manner. The peritonocula l h re were then ppre mated on ea h side er the pper row by ssgat sut re and the wound sealed. l int rupted out res lct cea serouscular on h side f the transect on. The ldom l woc d l owed in l h ers (Fig 5).

Con lence wa given ful. A normal bow l mo eme t ppassed on th h day. There did not pper he pperoxide mucous secretion from the lower blind segment f colon through the agnus.





Fig 3.—Photograph taken at operation showing T the vesicle, closely pyknot and exhibiting hyaline zone and (small granular) B in its descending and sigmoid aspect that shows as separate structures that no hyaline zone and the somewhat sperry similar to the of the small ves.



Fig 4.—A Photograph showing A, the two appendages and B, the two, both from the one. B Photograph showing the two, each with its appendage, and B, the two ascending vesicles.

At the operation just described no evidence of an abdominal tumor was observed. An explanation of the previous operative finding is that the inner sigmoid colon was filled and distended with fecal material. This explanation is supported by the fact that during the preoperative preparation for the last laparotomy it was very difficult to secure evacuation of this segment of the colon, which seemed to act as a reservoir for fecal material.

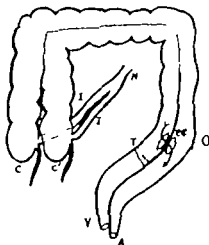


FIG. 1.—Diagram showing duplication of entire colon and lower segment of ileum as found at laparotomy in patient described as set V. Lower ileum divided into two separate segments, I. The ceca, A, each with appendix. If portions of ascending colon are separated but become closely approximated, there is danger here of partial separation. In some cases upper portion of descending colon here is separated beside sigmoid, O. Region of sigmoid here operation as performed is colo-cystostomy and T (transsection of normal sigmoid to share ileal material) but I (ileal loop) which entered it 4 months after setted about 1 vaginal anus. Both the lower colon terminated.

It is planned in the case described to postpone obliteration of the vaginal anus until later in life when the child has grown and the parts are larger and hence more easily handled. The lower end of the blinded segment of colon could be shunted into the lower functioning pelvic colon or this blinded segment could be resected completely as a more extensive procedure.

In September 1948, the patient remains well there is only a small mucous discharge from the vagina.

#### SUMMARY

The case of a female child with complete duplication of the colon including ceca, appendices, and lower ileum is presented. One of the colons terminated in a vaginal anus. The procedures in shunting all the fecal material into the normally situated colon in planus are described.

The anomaly appears to be quite rare as this is the eighth patient reported in the literature.

# GASEOUS DISTENTION OF THE LATEX BAG IN THE USE OF THE SINGLE LUMEN INTESTINAL TUBE

## ITS CAUSE AND PREVENTION

ALVIN E. LEWIS, M.D. AND WALTER LEFF, M.D. † SAN FRANCISCO, CALIF.

(From the Departments of Pathology and Surgery Mount Zion Hospital)

IN THIS clinical use of the Harris single lumen intestinal tube, several cases were encountered in which considerable difficulty was experienced in withdrawing the tube. The tubes were caught at either the ileocecal valve, pylorus, or just beyond the site of the partial obstruction. In these instances, after the tube was either forcefully withdrawn, allowed to pass per rectum, or removed at enterostomy, the latex bag was observed to be distended with gas. The purpose of the experiments reported here was to elucidate the mechanism of this distention with a view to formulating a satisfactory method for its prevention.

Since the bag became distended with no apparent source of gas other than its diffusion across the wall of the bag, it seemed probable that we were dealing with an osmotic phenomenon. The wall of the latex bag must then be permeable to one or more gases in the bowel and relatively impermeable to one or more gases in the air. The gas which diffused into the bag must be one which is present in low concentration in the air but in higher concentration within the bowel. Under these circumstances the permeable gas would diffuse into the bag until its partial pressure within the bag equalled its partial pressure within the bowel or until its diffusion was prevented by the counterpressure of the distended bag. If this explanation of the bag dilatation were true this distention could be prevented, regardless of the exact nature of the gases in the bowel lumen, by removing all traces of nondiffusible gases from the bag before its introduction into the bowel.

In order to test this explanation 4 c.c. of mercury were placed in a latex bag. This bag was then thoroughly flushed with carbon dioxide to remove all traces of air. The bag was then compressed to expel most of the gas, leaving the bag almost empty and simulating the condition of the bag as it is used clinically. A control bag was similarly prepared without being flushed with carbon dioxide. These bags were then suspended in an atmosphere of approximately pure carbon dioxide. Within one day the control bag became distended and tense while the bag which had been flushed with carbon dioxide remained in its initial collapsed and flaccid state. This experiment has been repeated several times, and the exposures were extended over a period of one month. The results were always identical with those of the first experiment. When the exposure was prolonged, there was never any significant change after the first day. These experiments were also performed with methane which was found to be relatively nondiffusible across the latex wall.

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## SUMMARY AND CONCLUSIONS

In the use of single lumen intestinal tubes utilizing rubber or latex bags weighted with mercury as a means of propulsion, the factors determining distention of the bag are (1) permeability of the latex bag (2) concentration of the diffusible gases in the bowel, and (3) the duration of the exposure within the bowel. The variations in these three factors undoubtedly account for the relative infrequency of complications due to excessive gaseous distention of the bag. However this complication can be entirely avoided in all cases if the latex bags are flushed with carbon dioxide before they are attached to the intestinal tube.

## ADDENDUM

Subsequent to the time that this paper was submitted for publication, papers by Cantor Phelps, and Elling on this same problem have been published. In their paper they reported the results of extensive quantitative investigation of the permeability characteristics of the various rubber balloons used on test animal tubes. It is gratifying to note that their studies completely substantiate our observations regarding the permeability of latex. They recommended the use of less permeable rubber bag (coprene-Q) tied firmly enough to prevent loss of the mercury, yet sufficiently loose to permit gases to escape. No doubt their method effect of their recommendations are carried out but we believe that the procedure of removing air from the balloon by flushing with carbon dioxide just prior to sealing them is simpler and more certain prevention of gaseous distention.

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In order to test this explanation, 4 c.c. of mercury were placed in a latex bag. This bag was then thoroughly flushed with carbon dioxide to remove all traces of air. The bag was then compressed to expel most of the gas, leaving the bag almost empty and simulating the condition of the bag as it is used clinically. A control bag was similarly prepared without being flushed with carbon dioxide. These bags were then suspended in an atmosphere of approximately pure carbon dioxide. Within one day the control bag became distended and tense while the bag which had been flushed with carbon dioxide remained in its initial collapsed and flaccid state. This experiment has been repeated several times, and the exposures were extended over a period of one month. The results were always identical with those of the first experiment. When the exposure was prolonged, there was never any significant change after the first day. These experiments were also performed with methane, which was found to be relatively nondiffusible across the latex wall.

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A



B



C

Fig 2 (Case 2).—A B and C C F. Merz Hospital operated upon Oct 22

burn

## ONLAY GAUZE PRESSURE DRESSING

PATRICK S. NAGLE, M.D. OKLAHOMA CITY, OKLA.

**S**KIN transplants are successfully held in situ by simple gauze pressure dressings tied on by peripherally placed long cotton sutures.

A skin transplant is accurately approximated to the prepared recipient area and carefully sutured margin-to-margin by interrupted No. 24 cotton sutures placed every one-quarter inch. These sutures are fourteen inches long and are tied in their midportion leaving two equal lengths which are laid back radially from the periphery.

Gauze is stuffed, folded, or rolled into a suitable mass to cover accurately the full perimeter of the skin transplant. This gauze is then appropriately encased by carefully wrapping with penicillin-benzocaine-lanolin impregnated gauze. This lanolin gauze is of moderate coarse mesh and is applied in a single and not a multiple thickness.



Fig. 1 (Case 1)—A and B.

University Hospital operated upon Oct. 12, 1941, resection of old tumor.

It is important that blood serum and pus may drain freely through the multiple perforations of the skin transplant and through the meshes of the grease gauze dressing to be absorbed by the overlying compressed gauze.

Additionally, it is important that the dressing overlying a skin transplant may breathe, that is to say, that the liquids absorbed by the gauze may evaporate into the atmosphere.

Received for publication, July 22, 1941.

If this function is not served by the dressing of the skin transplant, it will frequently macerate and undergo leucocytic digestion.

The onlay gauze dressing is compressed evenly against the skin transplant. By use of the preserved long cotton sutures this compression is maintained. Apposition sutures are tied firmly across the crown of the gauze mass. This dressing is undisturbed for fourteen days. When it is removed a simple dry dressing is adequate mechanical protection to the firmly adherent skin transplant.

This technique provides uniform unyielding non-slipping absorbent compression and protection to a wide variety of skin transplants either half thick new or full thickness.

It is adaptable to a wide variety of recipient sites. It is particularly adaptable to sites that are convex and irregular such as illustrated in Case 1 (Fig. 1). This technique is particularly efficient in sites where it is difficult to accomplish compression by the usual annular compression dressing such as in the neck, as illustrated by Case 2 (Fig. 2). In a situation of this kind annular compressing dressings are faulty. Ince by counterpressure they interfere with the veins in the the opposite side of the neck and if they pass under the arm they may embarrass the axillary nerves and axel. If the dressings are wound tightly around the neck, swallowing and respiration are interfered with.

Scalp defects are readily surfaced using the tied-on compression dressing to hold full thickness skin transplants in place. This is illustrated in Case 3 (Fig. 3). It is desirable to tailor these transplants to fit the defect exactly. Margin-to-margin approximation is important.

Case 4 (Fig. 4) illustrates one point and that is that this technique may be employed to hold split thickness skin transplants in place over granulating surfaces.

The Padgett dermatome is essential in the accomplishment of an even thickness autogenous transplant.

The development of this technique was a product of necessity. Upon returning to private practice two years ago, I found it impossible to secure a sufficient quantity of sea sponges. The few that were available were no larger than a tennis ball of poor quality and extremely costly. Mechanics waste and stuffed gauze have always given less even and more infirm pressure dressing than sea sponges.

It is my opinion based upon experience with the cases reported and others, that the tied in-place onlay gauze compression dressing gives better results when appropriately employed than do other forms of compression dressings.

Since his article as cited, it has been noted that several similar procedures are described in 19 by Mrs. Barrett Brown and Frank McDowell in the *XX Outline of* issue page 82, published by J. B. Lippincott Company.





Fig 3 (Case 3)—P D Ward, Hospital, operated upon May 14, 1947 for ill-cell carcinoma of the scalp



Fig 4 (Case 4)—B H B Merty Hospital, operated upon Dec 4 1947 granulating burned area of dorsum of the hand

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The Padgett dermatome is essential in the accomplishment of an even thickness autogenous transplant.

The development of this technique was a product of necessity. Upon returning to private practice ten years ago, I found it impossible to secure a sufficient quantity of sea sponges. The few that were available were no larger than a tennis ball of poor quality and extremely costly. Mechanics waste and stuffed gauze have also been given a less even and more firm pressure dressing than sea sponges.

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Fig 3 (Case 3)—R D Wesley Hospital operated upon May 14, 1957 basilo-carcinoma of the scalp



Fig 4 (Case 4)—B H B Merry Hospital operated upon Dec 4, 1957 granulating burned area of dorsum of the hand

**Second Episode**—The patient admitted to Jeffeson Hospital on May 1 1946, at the age of 50 years. Within the preceding two months he had experienced increasing weakness and fatigability, loss of ten pounds in weight, and pain in the upper third of the right arm. The pain was dull, boring, intermittent, lasting for one or two hours and aggravated by activity. Despite these symptoms he had continued work until admission.

Physical examination revealed a healed vertical scar along the anterior margin of the left sternocleidomastoid muscle. The thyroid gland just palpable but no nodules were felt. There was deep tenderness over the lateral aspect of the upper fifth of the right arm. The left lower extremity was two inches shorter than the right. No slight limitation of external rotation.

The blood count revealed moderate secondary anemia. Urinalysis except for fixed specific gravity of 1.00 to 1.009 normal. The blood urea nitrogen was 10.0 mg per 100 ml and creatinine 1.7 mg per 100 ml. Urea clearance was 40 per cent of normal. Serum calcium was 15.8 mg per 100 ml, serum phosphorus 1 mg per 100 ml, and alkaline phosphatase 63 Bodansky units.



Fig. 1.—Gross specimen and photomicrograph, chief cell adenoma of the parathyroid gland (X250).

Roentgenographic study of the entire skeleton revealed general demineralization of all the bones, with gross appearance of the calcareous. A large cyst as noted in the neck of the right scapula, as well as cystic areas in the right ilium and the right femoral neck and trochanteric region and left tibia. There was considerable abnormal calcification in both kidneys.

At operation on May 16, 1946, using nitrous oxide and general anesthesia, the patient's thyroid region was explored. Exposure and palpation of the usual sites of the parathyroid glands, including the site of the previous adenoma, revealed no abnormalities. Subtotal exploration disclosed a nodule at the right of the esophagus and behind the recurrent laryngeal artery. The tumor was dark red, firm, free of the artery which crossed it.

On the first postoperative day the serum calcium was 6 mg per 100 ml and serum phosphorus 1 mg per 100 ml. On the fourth day the first experienced tingling of the hands and mouth, feeling of pressure in the anterior thoracic region and mild horripilation.

## Case Reports

### PARATHYROID ADENOMA

#### OCCURRENCE IN FATHER AND DAUGHTER

THOMAS A. SHALLOW, M.D., AND KENNETH E. FRY, M.D., PHILADELPHIA, Pa.

(From the Russell D. Gross Surgical Division of the Jefferson Medical College Hospital)

THE unique occurrence of parathyroid adenoma in father and daughter has not previously been reported. The father's case alone is of outstanding interest because he suffered two episodes of hyperparathyroidism separated by an interval of fifteen years. The unusual aspects of these two cases, as well as the long periods of follow-up obtained, warrant their report in some detail.

#### CASE REPORTS

##### FATHER—C. F.

*Pat. Pseud.*—C. F., physician, aged 53 years, as seen in bed at home by one of us (T. A. S.) in November 1931. At this time he was convalescing from spontaneous fractures of the surgical neck of the right humerus and comminuted sternoclavicular fractures of both femurs, sustained on Sept. 23, 1931, while walking steps. The fractures had been reduced at Montgomery Hospital, Norristown, Pa. Stated: Done during this admission in 1927 mild secondary anemia, occasional trace of albumin in the urine and traces of Bruce Jones protein in the urine. The roentgenograms showed bone changes suggestive of extensive fibrous erosion or multiple myeloma.

Inquiry into the patient's past history disclosed that in 1925, at the age of 49 years he had experienced symptoms of diastolic sleep proved by roentgenograms. In 1927 in addition to the gastrointestinal symptoms he had polyuria and polydipsia of such severity that diabetes mellitus was suspected. In 1929 he became nervous and irritable. In 1931 he lost weight but he described himself as healthy. In July of that year he began to experience constant boring pain in all the extremities, more in the right. During the four-year period from 1927 to 1931 he lost forty pounds.

Physical examination revealed a poorly nourished 53-year-old man obviously emaciated because of multiple fractures. A mass palpable in the region of the lower pole of the left lobe of the thyroid gland. The remainder of the physical examination as normal. Preliminary A. prescriptive diagnosis of parathyroid adenoma as made and operation advised.

The patient was readmitted to Montgomery Hospital on Dec. 22, 1931. The preoperative laboratory studies showed no change, and the serum calcium as 13.0 mg. per 100 ml. Operation was performed on Dec. 24, 1931, using 1 per cent novocaine local infiltration. A tumor removed from the region of the lower pole of the left thyroid lobe. The sites of the other parathyroid glands were palpated but no enlargement could be detected. The patient's

It measured 3.2  
adenoma composed

of sheets of amorphous cells supported by a cellular, richly vascularized stroma. During the ensuing year the patient's health gradually improved. The fractures healed, he gained forty pounds in weight, and acquired his former vigor. He returned to active practice in June 1932, and continued without symptoms until March, 1934.

Received for publication, Jan. 24, 1934.

**Second Episode**—The patient was admitted to Jefferson Hospital on May 1, 1944, at the age of 50 years. Within the preceding two months he had experienced increasing weakness and fatigability, loss of ten pounds in weight, and pain in the upper third of the right arm. The pain was dull, boring, intermittent, lasting for one or two hours, and aggravated by activity. Despite these symptoms he had continued work until admission.

Physical examination revealed a well-built man with long, straight, brown hair. The thyroid gland was not palpable, but no nodules were felt. There was deep tenderness over the lateral aspect of the upper fifth of the right arm. The left lower extremity was two inches shorter than the right with slight limitation of external rotation.

The blood count revealed moderate secondary anemia. Urinalysis except for a fixed specific gravity of 1.007 to 1.009 was normal. The blood urea nitrogen was 10.0 mg per 100 ml and creatinine 1.7 mg per 100 ml. Urea clearance was 40 per cent of normal. Serum calcium was 15.8 mg per 100 ml, serum phosphorus 4.1 mg per 100 ml, and alkaline phosphatase 6.3 Bodansky units.



Fig. 1.—Gross specimen and microphotograph, oxyphil and chief cell adenoma of the parathyroid gland ( $\times 200$ ).

Radiogenographic study of the entire skeleton revealed general demineralization of all the bones, with a grainy appearance of the calvarium. A large cyst was noted in the neck of the right scapula, as well as cystic areas in the right ulna, several ribs, the right femoral neck, and tracheosternal region and left ilium. There was considerable bony calcification in both kidneys.

At operation, on May 16, 1946, using nitrous oxide or gas ether anesthesia, the patient's thyroid region was explored. Exposure and palpation of the usual sites of the parathyroid glands, including the site of the previous adenoma, revealed no abnormalities. Subtotal exploration disclosed a small, dark, right of the esophagus and behind the recurrent laryngeal nerve. The tumor was delivered after freeing the nerve which crossed its center.

On the first postoperative day the serum calcium was 9.6 mg per 100 ml and serum phosphorus 1 mg per 100 ml. On the fourth day he first experienced tingling of the hands and mouth, feeling of pressure in the anterior thoracic region, and mild shortness of breath.

of breath. The symptoms of hypoparathyroidism were subsided by serum calcium of 7 mg per 100 ml. The serum phosphorus 3 mg per 100 ml. On the eleventh day the serum calcium was 7.0 mg. per 100 ml. and serum phosphorus 2.6 mg per 100 ml. despite the fact that the patient's symptoms were controlled by administration of calcium lactate and vitamin D. The patient was discharged June 1, 1946 on the sixteenth postoperative day. At this time the wound was well healed and the mild symptoms of tetany were easily abolished by oral administration of calcium lactate.

The gross and microscopic features of the tumor are shown in Fig. 2. It was well capsulated and measured 4.2 by 3.6 by 3 cm. Microscopically it was parathyroid adenoma in which the neoplastic cells were of the water-clear type and typical anastomosing cords.

The patient failed to improve following discharge from the hospital. Appetite was poor, he lost weight, and the family noted retardation in his memory and word association. He experienced no symptoms of tetany. Lower and serum calcium determination on June 20, 1946 revealed 8.7 mg per 100 ml.



Fig. 2—Gross specimen of parathyroid adenoma of the parathyroid gland, mixed cell variety (X200).

The patient was readmitted to Jefferson Hospital in October of 1946, on which date he vomited for the first time. The temperature was 101.2° F, pulse rate 94 per minute and respirations 24 per minute. Detailed neurologic examination revealed no evidence of localized lesion. The blood urea nitrogen was 40.0 mg per 100 ml, creatinine 4 mg per 100 ml, 30 per cent bromsulphalein dye retained at the end of 30 minutes, Van der Berg positive direct with serum bilirubin 2.4 mg per 100 ml and serum alkaline phosphatase 400 units. Serum calcium was 8.0 mg per 100 ml, serum phosphorus 4.5 mg per 100 ml and alkaline phosphatase 94 Bodansky units. Spinal fluid was under normal pressure and revealed no abnormalities.

The patient's condition improved following administration of fluids, intravenous glucose, protein, vitamins, and calcium lactate. On Aug. 22, 1946, the blood urea nitrogen

was 7.4 mg per 100 ml. Appetite decreased, he gained weight, and became heariscentally ill. He was discharged to his physicians care Aug 4 1946. The patient died suddenly on April 20, 1947 from what appeared to be cerebral hemorrhage. Nephrectomy was performed.

**DAUGHTER'S CASE**—M. F. aged 14 years was admitted to Jefferson Hospital on Aug 1, 1939 with the chief complaint of loss of stamina and change of gait. Seven months prior to admission she began to experience increasing weakness after light exertion. At the same time she gradually developed change of gait which as not improved by edging of her shoes. One month prior to admission, the mother learned that the daughter's gait resembled the huffling gait of the father eight years previous. Outpatient laboratory studies revealed that serum calcium was 13.4 mg per 100 ml serum phosphorus 1.8 mg per 100 ml and alkaline phosphatase 6 Bodansky units.

One year prior to admission the patient had sustained fracture of the surgical neck of the left humerus following severe fall. Roentgenograms at that time revealed no underlying bone disease and the fracture healed normally.

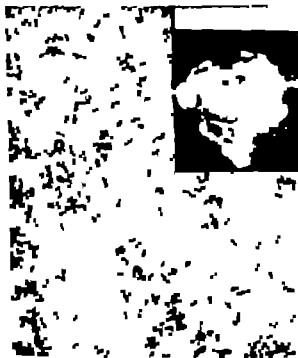


Fig 2.—Gross specimen and microphotograph of parathyroid gland predominantly chief cell cysts (X 44).

Physical examination revealed that the patient had an otic gait resembling the waddling of a duck. The remainder of the physical examination was negative except that palpation in the region of the lower pole of the left thyroid lobe revealed small regular masses which moved with deglutition.

Repeat blood chemistry determinations were essentially the same as those just prior to admission. In addition, the blood count revealed normal blood urea nitrogen and serum proteins were within normal limits. Roentgenologic studies of the skeleton revealed demineralization of all the long bones and calcification with sclerosis and increased density in the metaphyseal regions.



f breath. The symptoms of latent tetany subsided by serum calcium of 7.7 mg per 100 ml. The serum phosphorus was 3.2 mg. per 100 ml. On the eleventh day the serum calcium was 7.0 mg per 100 ml. and serum phosphorus 3.6 mg per 100 ml. Despite the fact that the patient's symptoms were controlled by administration of calcium lactate and vitamin D. The patient was discharged June 1, 1946, on the sixteenth postoperative day. At this time the wound was well healed and the mild symptoms of tetany were easily abolished by oral administration of calcium lactate.

The gross and microscopic features of the tumor are shown in Fig. 2. It was well encapsulated and measured .43 by .6 by .2 cm. Microscopically it was parathyroid adenoma, which the epithelial cells were of the waterbury type and typical variety.

The patient failed to improve following discharge from the hospital. Appetite was poor, he lost weight and the family noted retardation in his memory and relaxation. His experience had no symptoms of tetany been and serum calcium determination on June 20, 1946, revealed 8.7 mg per 100 ml.



Fig. 2—Gross specimen and microphotograph adenoma of the parathyroid gland stained with hematoxylin and eosin (H&E).

The patient was readmitted to Jefferson Hospital on July 10, 1946, on which day he was operated on for the first time. The temperature was 101.2° F, pulse rate 94 per minute, and blood pressure 120/80 mm. Hg. A serum examination revealed no calcium, no phosphorus, and no alkaline phosphatase. The serum calcium was 6.8 mg per 100 ml. and serum phosphorus was 3.6 mg per 100 ml. The patient was given normal pressure and

fluids extra carefully. The patient was given glucose, protein, vitamins, and calcium lactate. On July 10, 1946, the blood urea nitrogen

was 29.4 mg per 100 ml. Appetite increased, he gained weight, and became less mentally depressed. He was discharged to his physician's care on Aug. 4, 1946. The patient died suddenly on April 20, 1947 from what appeared to be a cerebral hemorrhage. Autopsy was performed.

**DISCUSSION.** CASE.—M. F., aged 44 years, admitted to Jefferson Hospital on Aug. 1, 1939 with the chief complaint of loss of stamina and fatigue of past seven months prior to admission. She began to experience increasing weakness after light exertion. At the same time she gradually developed change of gait such as not improved by edging of her shoes. One month prior to admission, the mother learned that the daughter gait resembled the huffling gait of the father. gait ears protruded. Outpatient laboratory studies revealed that serum calcium was 15.4 mg per 100 ml, serum phosphorus 1.9 mg per 100 ml, and alkaline phosphatase 6 Bodansky unit.

One year prior to admission the patient had a nonunion fracture of the surgical neck of the left humerus following a severe fall. Roentgenograms at that time revealed no underlying bone disease, and the fracture healed normally.

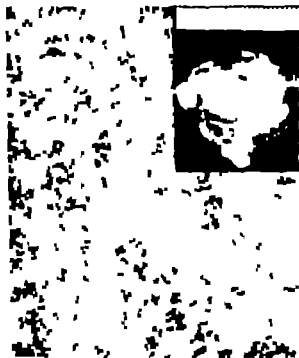


Fig. 3.—Owen specimen and microphotograph adenoma of the parathyroid gland, predominantly chief cell area. (×240)

Physical examination revealed that the patient had a stooped gait, resembling the waddling of duck. The remainder of the physical examination was negative except that palpation of the region of the lower pole of the left thyroid lobe revealed a small, regular mass which moved with deglutition.

Repeat blood chemistry determinations were essentially the same as those just prior to admission. In addition, the blood eosinophil count, urea nitrogen, blood urea nitrogen, and serum proteins were within normal limits. Roentgenologic studies of the skeleton revealed demineralization of all the long bones and calcium, with fusiform and increased density in the metaphaseal regions.

At operation on Aug. 9 1939 using orthotrioxymide nitrogen and ether anesthesia a parathyroid adenoma was removed from the region of the inferior pole of the left lobe of the thyroid. Careful palpation of the other parathyroid areas revealed no abnormalities.

On the sixth postoperative day the patient serum calcium was 9.0 mg per 100 ml, serum phosphorus 2.5 mg per 100 ml and alkaline phosphatase 17 Bodansky units. Repeat of these studies on the fourth day revealed serum calcium 9.5 mg per 100 ml, serum phosphorus 2.7 mg per 100 ml and alkaline phosphatase 1.5 Bodansky units. The patient's condition was uneventful, and he was discharged on the fifteenth day.

The gross and microscopic features of the tumor are shown in Fig. 3. It measured 7 by 2.5 by .5 cm. Microscopically it was parathyroid adenoma mainly of the chief cell variety although there were few small foci of oxyphil cells.

Complete follow-up examination of the patient on Nov. 10 1940 three months after operation revealed marked improvement. Gait had become normal, she had much more stamina, and was attending school regularly. Blood chemistry studies revealed serum calcium 10.2 mg per 100 ml serum phosphorus 3.1 mg per 100 ml and alkaline phosphatase of 14.0 Bodansky units. Roentgenologic study showed a slight resorption of all the long bones and the metacarpal regions of the radius and ulna of the wrist joint were more normal.

On April 12, 1941 ten years and eight months after operation, the patient was again examined and all respect was the normal controls.

#### DISCUSSION

In an analytical review of 32 cases of parathyroid adenoma by Norris, collected from 1903 to 1943 inclusively no mention is made of the occurrence of this tumor in members of a family. Although the development of the disease in our two patients in such close blood relatives may have been a mere coincidence, the possibility is at least suggested that in certain instances it might have a familial tendency. Schneider Kyger and McNally recently reported its occurrence in second cousin once removed.

The father developed symptoms of parathyroid adenoma not long after the first reported surgical removal of a parathyroid adenoma by Mandl, but was not operated upon until four years later following three spontaneous fractures. Removal of the adenoma in 1931 permitted such an improvement in his condition that he apparently was normal. The second adenoma, located subinternally on the opposite side did not produce symptom for fifteen years. Whether the subinternally adenoma was present at the time of the first operation in latent form and gradually became more active or whether it developed rapidly years later is uncertain. It is evident, however that the hyperparathyroidism was primary and not secondary hyperplasia due to renal insufficiency. Renal damage was not manifested until the time of the second operation, fifteen years later. This was secondary to the hyperparathyroidism, as shown by roentgenologic demonstration of considerable calcification in both kidneys. At this time the blood urea nitrogen was normal, although the urine showed a low fixed specific gravity and the urea clearance was only 40 per cent of normal. With removal of the second adenoma the patient developed hypocalcemic tetany hepatorenal failure, and died eleven months later from what appeared to be cerebral hemorrhage. The hyperphosphatemia developed on the basis of triam and also phosphate retention on the basis of renal failure. Death from a vascular accident is in keeping with the disease because of the abnormal deposition of calcium

in the arteries. Although the history of the second episode dated back only two months, the irreparable damage caused by the disease is evidence that the hyperparathyroidism had probably existed insidiously and asymptotically over a period of years.

It is interesting that the mother first suggested the diagnosis of parathyroid adenoma in the daughter because of the resemblance in gait to that of the husband in 1931. The fracture which occurred one year prior to the daughter's operation was probably not a pathologic one since sufficient trauma was acknowledged and the roentgenogram showed no evidence of underlying bone disease. The subsequent roentgenographic findings were minimal consisting chiefly of generalized skeletal demineralization. The prompt return of the blood calcium and phosphorus to normal following removal of the adenoma confirmed the diagnosis. The other siblings in this family showed no evidence of disturbance in calcium and phosphorus metabolism.

#### CONCLUSIONS

1. Parathyroid adenoma may occur in blood relatives. This suggests that in certain instances search should be made for evidence of disturbance in calcium and phosphorus metabolism in other members of the family.

Patients who have undergone surgical excision of a parathyroid adenoma should be checked periodically as long as they live since it is possible for a second adenoma to develop.

The authors are grateful for the cooperation of Dr. Peter A. Herbut in reviewing the pathological material.

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At operation on Aug 9 1930 using vertical nitrous oxide oxygen and ether anesthesia, parathyroid adenoma was removed from the region of the inferior pole of the left lobe of the thyroid. Careful palpation of the other parathyroid sites revealed no abnormalities.

On the sixth postoperative day the patient's serum calcium 8.0 mg per 100 ml serum phosphorus 5 mg per 100 ml and alkaline phosphatase 17 Bodansky units. Repeat of these studies the fourteenth day revealed serum calcium 9.5 mg per 100 ml serum phosphorus 2.7 mg per 100 ml and alkaline phosphatase of 125 Bodansky units. The patient's convalescence was successful and she was discharged on the fifteenth day.

The gross and microscopic features of the tumor are shown in Fig 3. It measured 7 by 2.5 by 1 cm. Microscopically it was a parathyroid adenoma mainly of the chief cell variety although there were few small foci of oxyphil cells.

Complete follow-up examination of this patient on Nov 10 1930 three months after operation revealed marked improvement. Gait had become normal, she had much more stamina, and was attending school regularly. Blood chemistry studies revealed serum calcium 10 mg per 100 ml serum phosphorus 3.1 mg per 100 ml and alkaline phosphatase of 140 Bodansky units. Roentgenologic study showed definite remineralization of all the long bones, and the metaphyseal regions of the radius and ulna and the wrist joints were more normal.

On April 1, 1947 seven years and eight months after operation the patient was again examined and all respects with normal limits.

#### DISCUSSION

In an analytical review of 32 cases of parathyroid adenoma by Harris, collected from 1903 to 1941, inclusion of no mention is made of the occurrence of this tumor in members of a family. Although the development of the disease in our two patients in such close blood relatives may have been a mere coincidence, the possibility is at least suggested that in certain instances it might have a familial tendency. Schneider Hyger and McCullagh recently reported its occurrence in second cousins once removed.

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in the arteries. Although the history of the second episode dated back only two months, the irreparable damage caused by the disease is evidence that the hyperparathyroidism had probably existed insidiously and asymptotically over a period of years.

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The authors are grateful for the cooperation of Dr. Peter A. Herbst in reviewing the pathological material.

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# POLYPS OF THE SIGMOID OCCURRING THIRTY YEARS AFTER BILATERAL URETROSIGMOIDOSTOMY FOR ECTROPY OF THE BLADDER

## REPORT OF A CASE

CLAUDE F. DIXON, M.D. AND RODGER E. WITTMANN, M.D. † ROCHESTER, MINN.

**TRANSPLANTATION** of ureters into the rectosigmoid or sigmoid flexure of the colon has received universal acceptance in the past twenty years. There has been an increasingly wider application of some form of this operative procedure in the treatment of certain serious benign and malignant lesions of the lower part of the urinary tract. Late results are of considerable interest and importance in determining the ultimate usefulness of ureterosigmoidal anastomosis.

Advances in diagnostic and clinical methods of preoperative evaluation of both the urinary and gastrointestinal systems have aided in the proper selection of candidates for this type of operation. The operative morbidity and mortality have been sharply decreased since prophylactic and therapeutic use of the newer chemotherapeutic and antibiotic preparations and other valuable preoperative and postoperative measures. In recent years some workers have stated that bilateral ureterosigmoidostomy and total cystectomy can be accomplished in a one-stage procedure as safely as it formerly was in a three-stage procedure. It would seem, however, in most instances that the multiple-stage procedure is the safer.

Ureterocolonic anastomosis, as used in the surgical treatment of ectropny of the bladder, was materially advanced by contributions of Maydl,<sup>1</sup> Moynihan,<sup>2</sup> Bergenhem,<sup>3</sup> Peters,<sup>4</sup> Coffey,<sup>5</sup> and Mayo<sup>6</sup> and associates.<sup>7</sup> Its feasibility was demonstrated by these earlier investigators. In the Maydl procedure as modified by Moynihan, a portion of all of the trigones of the bladder with the ureterovesical valves anatomically intact, but with their nerve supply interrupted, is transplanted to the wall of the rectosigmoid. In the Bergenhem procedure, later modified by Peters, each ureter with a cuff of adjacent vesical wall is transplanted separately into the distal portion of the sigmoid. These two procedures have been almost entirely abandoned not only because of technical difficulties, but also because of the fecal remnant which, as will be shown later, frequently may be the site of malignant change. The concepts and surgical principles originally described by Coffey have largely become the basis for the present-day surgical procedures. Many modifications have been introduced which have reduced operative mortality and contributed to more satisfactory end results.

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## POSTOPERATIVE CHANGES IN KIDNEYS

During the immediate and early postoperative phase the presence of a serious ascending renal infection with subsequent renal insufficiency due to ureteral obstruction or atony or both, formerly accounted for most of the operative morbidity and mortality after ureteral intestinal anastomosis. Some degree of pyelitis, ureterectasis, or both, usually was observed in the earlier series. In more recent reports Walters and Brunsch<sup>1</sup> stated that little dilatation of the upper part of the urinary system should occur and, consequently, little infection. In seventy-six cases upon which they reported, only one death was caused by renal infection. In their follow-up study of seventy-nine ureteral transplants, Marshall and Gardner<sup>2</sup> reported that only four ureters failed to function properly after the patients were dismissed from the hospital. Ladd and Gross<sup>13</sup> reported that in twenty-six children operated on for exstrophy only one child subsequently required nephrectomy for unilateral hydronephrosis and renal damage. Jodigian and Bickers<sup>14</sup> reported that of seventeen patients who survived uretero-sigmoidal anastomosis, only one was readmitted subsequently for acute pyelitis.

In cases of ureteral transplantation for benign conditions, the outlook for good renal function over a period of many years is apparently good. Many of the patients who underwent the operation at the Mayo Clinic have been observed for more than twenty years.

## POSTOPERATIVE EFFECTS ON THE COLON OR RECTUM

Except for the technical problems of anastomosis into the colon and those connected with the presence of myriads of pathogenic organisms in the contents, the sigmoid and rectum have not presented any serious obstacles to the development of the present operative procedures of ureteral colonic anastomosis. The distal part of the colon and the rectum are able to readjust remarkably well in practically all instances, to the physical and chemical alterations of the contents occasioned by the constant influx of urine. Significant pathologic disorders of the bowel as a result of the presence of urine have apparently not been encountered heretofore. Furthermore, the incidence of diseases common to that portion of the bowel is not appreciably influenced by the presence of urine. There is no evidence that significant absorption of products of urinary excretion occurs from the distal part of the sigmoid or the rectum.<sup>15</sup>

The occurrence of glandular polyps in the sigmoid or rectum in a case in which unilateral or bilateral ureteral transplant into the distal part of the colon was accomplished is apparently extremely rare. In a careful search of the literature we are unable to find a report of a case similar to ours. Hammer<sup>16</sup> in 1929 reported a case of carcinoma of the sigmoid in a 60-year-old man who had undergone ureterovesicosigmoidostomy after the method described by Maydl. The operation was done ten years previously for exstrophy of the bladder. The lesion in Hammer's case was probably primary in the transplanted vesical remnant. Reference will be made later to this report.

In 1919 Mayo presented a remarkable series of twenty-six cases of exstrophy of the bladder in which the patients were operated on at the Mayo Clinic from



# POLYPS OF THE SIGMOID OCCURRING THIRTY YEARS AFTER BILATERAL URETEROSIGMOIDOSTOMY FOR EXSTROPHY OF THE BLADDER

## REPORT OF A CASE

CLAUD F. DIXON, M.D. AND RODGER E. WITTMANN, M.D. † ROCHESTER, MINN.

**T**RANSPLANTATION of ureters into the rectosigmoid or sigmoid flexure of the colon has received universal acceptance in the past twenty years. There has been an increasingly wider application of some form of this operative procedure in the treatment of certain serious benign and malignant lesions of the lower part of the urinary tract. Late results are of considerable interest and importance in determining the ultimate usefulness of ureterosigmoidal anastomosis.

Advances in diagnostic and clinical methods of preoperative evaluation of both the urinary and gastrointestinal systems have aided in the proper selection of candidates for this type of operation. The operative morbidity and mortality have been sharply decreased since prophylactic and therapeutic use of the new chemotherapeutic and antibiotic preparations and other valuable preoperative and postoperative measures. In recent years some workers have stated that bilateral ureterosigmoidostomy and total cystectomy can be accomplished in a one-stage procedure as safely as it formerly was in a three-stage procedure. It would seem, however, in most instances that the multiple-stage procedure is the safer.

Uterocolonic anastomosis, as used in the surgical treatment of exstrophy of the bladder, was materially advanced by contributions of Maydl,<sup>1</sup> Moynihan,<sup>2</sup> Bergenhem,<sup>3</sup> Peters,<sup>4</sup> Coffey,<sup>5</sup> and Mayo<sup>6</sup> and associates. Its feasibility was demonstrated by these earlier investigators. In the Maydl procedure, as modified by Moynihan, a portion or all of the trigone of the bladder with the ureterovesical valves anatomically intact but with their nerve supply interrupted, is transplanted to the wall of the rectosigmoid. In the Bergenhem procedure later modified by Peters, each ureter with cuff of adjacent vesical wall is transplanted separately into the distal portion of the sigmoid. These two procedures have been almost entirely abandoned not only because of technical difficulties, but also because of the residual remnant which, as will be shown later, frequently may be the site of malignant change. The concepts and surgical principles originally described by Coffey have largely become the basis for the present day surgical procedures. Many modifications have been introduced which have reduced operative mortality and contributed to more satisfactory end results.

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Excretory urogram showed that the left kidney was nonfunctioning and that the right kidney was normal except for a mild horseshoe type of deformity.

Concentration of hemoglobin was 11 Gm per 100 of blood with erythrocytes numbered 3,350,000 and leucocytes 8,000 per cubic millimeter of blood. The sedimentation rate was 81 mm per hour (Westergren). The basal blood urea was 30 mg per 100.

A roentgenographic examination of the thorax revealed no abnormalities. Result of the flocculation test of the blood for syphilis was negative.

Because of the recurrent attacks of pain, chills, and fever and the loss of function of the left kidney (demonstrated by retrograde pyelography), it was decided that left nephrectomy should be carried out. On Dec. 30, 1946, exploration of the left kidney was made through a left post-columba incision and it was found to be enlarged and thickened. A rather extensive inflammatory condition was present in the perinephric fat. At this site there were spermatozoa. The vessels around the ureter were dilated but otherwise were in good condition. The kidneys were removed and three ties were placed on the renal pedicle and one on the distal stump of the ureter. The pathologist reported that 15 cm. of ureter was removed with the kidney and that the kidney weighed 305 grams. The pathologic diagnosis was pyelonephritis and hydronephrosis. The postoperative course was uneventful. Discharge from the hospital was given on the fourteenth postoperative day.

After the patient was released from the hospital roentgenographic studies of the colon revealed a polypoid lesion in the sigmoid. The distal lesion was about 5 cm. in diameter and was thought to be the one observed previously in the course of proctoscopic examination. The proximal lesion was at the junction of the sigmoid and descending colon; it was estimated to be about 7 cm. in diameter. Just distal to this tumor the roentgenologic findings showed annular constriction, the nature of which was not determined but it was thought to be neoplastic. The remainder of the colon was normal. Further proctoscopic biopsy was made at a level about 30 cm. below the anus but no lesion was found other than those previously demonstrated.

The patient admitted to the hospital for preparation for colon operation. This preparation consisted of giving a residue-free diet with oxidized (sucrinate) sulfathiazole orally and daily colon irrigations for four days. At the time of admission the concentration of hemoglobin was 13 Gm per 100 and erythrocytes numbered 4,550,000 per cubic millimeter. On July 31, 1947, exploration of the abdomen was carried out through a primary left rectus muscle splitting incision. Two polypoid lesions were found in the sigmoid, depicted by the roentgenologic studies. The gall bladder, stomach, and remainder of the colon appeared to be normal. Palpation of the remaining right kidney revealed that it was enlarged to about as big as half the normal size, the lower pole swinging upward and medially, suggesting a complete horseshoe deformity. Through

a transverse long incision in the wall over the colon on rising to the large proximal polypoid lesion and excised a portion of the mucosa and submucosa at this place. The stump of the left ureter had to be descending colon just proximal to the lesion and was sutured. Exploration of the colon showed that the base of the polypoid lesion did not show the exact location of the neck of the tumor. The bowel

lower transverse colon was rows of brownish gut suture. The small distal sigmoidal polyp was exposed. Similar was seen just below the rectosigmoid. Before proceeding with removal of the lesion the right ureter was sutured and the site of the transplant to the lower part of the sigmoid was carefully determined. It was found that the polyp arose from the mucosa of the sigmoid. The site of the right ureter previously transplanted into the bowel. The pedicle was transected with much care with the probe. The right ureter, hemostasis obtained without difficulty by means of carefully placed sticks in the mucosa and submucosa of the colon below the ureteral orifice. The bowel was given lower transverse incision in the lower part of the brownish gut suture 5 Gm. of sulfathiazole and 100 Gm. of penicillin were left in the abdominal cavity before the wound was closed in layers.

1912 through 1910. He employed a modification of the Coffey I technique. Operation was considered successful in twenty two cases at the time of our report. The case we are reporting is one of this series.

The patient in the following case was recently observed and treated at the Mayo Clinic. Polyps were found in the sigmoid colon thirty years after successful bilateral ureteroinguinal anastomosis and cystectomy or cystostomy of the urinary bladder. The case is reported because of the unusual nature and importance of this complication.

#### REPORT OF A CASE

The patient, single 23-year old consultant research engineer was first examined at the Mayo Clinic, Sept. 30, 1916, at the age of 2 years. At the early admission he had ectrophy of the bladder and marked deformity of the penis and scrotum of congenital nature. The only complaints were those associated with the existence of congenital defects of urination. On physical examination it was found that he was otherwise normal and well developed child. There was typical ectrophy of the bladder with complete epispadias and a bifid scrotum containing both testes. Roentgenologic examination of the pelvis showed bilateral hydronephrosis of the medial portions of the pelvical calyces. Concentration of hemoglobin was 74 Gm per 100 of blood. Results of the laboratory tests were within normal limits.

On Sept. 27, 1916 the right ureter was transplanted into the lower rectal region of the rectosigmoid using the transperitoneal Coffey I procedure. The left ureter was similarly transplanted on Oct. 14, 1916, into the upper sigmoid. On Oct. 21, 1916, excision of the mucous membrane and muscularis of the ectrophied bladder and portion of the abdominal wall was made. Urinary leakage from all three placed ureters was successful and the patient was discharged from the hospital on Nov. 18, 1916.

Subsequently the patient developed usually mild but complete weakness of degree increasing from infancy.

In 1941 he noticed attack of pain in both costovertebral angles and flanks associated with chills, fever and headache. These episodes continued to occur with increasing frequency and in the course of most of them he was hospitalized and given courses of sulfonamide therapy. In November 1946, about one month prior to return to the Mayo Clinic, he had another attack of pain in both costovertebral angles with chills, fever, headache and malaise. He was given a course of treatment with sulfonamides and thereafter symptoms were relieved. He had two further similar less severe attacks during the interval before registration at the Mayo Clinic on Dec. 4, 1946. Further investigation of his history revealed that he had observed some bright red blood in the stools (October 1946) and that at that time he had consulted a proctologist who made diagnoses of small rectal polyp and advised removal. The patient stated that he had had rectal acutiae without associated symptoms approximately every three hours during the day but that prior to admission he had had occasional cramping pain in the lower midabdomen associated with bowel movements. In addition, he had lost approximately twenty pounds (9.1 kilo grams) in weight.

Physical examination at the second admission revealed a well developed man who did not appear particularly ill. There was slight tenderness in the left costovertebral angle. Bilateral lower abdominal paramedian scars of previous operations were present in the abdominal wall. There was fairly marked swelling and herniation about 6 cm in diameter in the suprapubic region at the site of excision of the ectrophied bladder. The persistent penile deformity consisted of rudimentary duplicated glans and epispadias at its base. The scrotum was small and infarcted but the testes were normal on palpation. With the exception of the presence of mild distention of the rectum no abnormalities were detected on digital examination of that structure. Proctoscopic investigation revealed a polyp on the right anterior wall of the rectosigmoid approximately 16 cm from the anus.

diet on the fifth postoperative day. At the time of dismissal from the hospital he was upon a full diet and colon function was normal. On the eighth postoperative day a mild superficial wound infection developed and subsided within a few days and local treatment. Release from the hospital was on February 1, 1941, at which time he was in good condition.

The patient reported by correspondence one month postoperatively that he was in splendid health, had regained his normal weight, and was able to carry on his usual occupation and athletic activities.



Fig. 3.—The smaller distal lesion: benign glandular structures in substance of the polyp and the surface covered with colonic epithelium (hematoxylin and eosin,  $\times 50$ ).

#### COMMENT

The presence of unilateral pyelonephritis, nonfunctioning kidney and polypoid sigmoidal lesions is of considerable interest and significance in this case. Renal complications of this nature are, unfortunately, a common early postoperative development. On the other hand, loss of function in previously normal kidneys many months or years after ureterosigmoidostomy occurs much less frequently. Few long-term studies are available to ascertain with any certainty the incidence of very late renal complications. A check of the record of cases at the Mayo Clinic reveals an instance of protracted loss of function in an undiseased kidney after dismissal following ureterosigmoidostomy.

The history in this case suggests that the pathologic changes in the left kidney may have been due to repeated episodes of ureteral obstruction, pyelonephritis, both for a period of five years. The anatomic proximity of both sigmoidal lesions to the respective ureteral orifices would strongly indicate that one or both could produce enough intermittent complete or partial obstruction to account for the renal disease. It is likely that the proximal sigmoidal polyp, since it was the larger, was present for a longer period of time and had produced the mechanical effects on that portion of the sigmoid, involving the left ureteral opening. This is a probable explanation of why the left kidney showed the

The pathologist reported that the first tumor was grade 1 adenocarcinoma—an adenoma, 4 cm. in diameter. The stalk of the adenoma was not involved. The second tumor was hyperplastic adenomatous polyp 2 cm. in diameter. The gross and histologic characteristics of the two lesions are shown in Figs. 1 to 3.

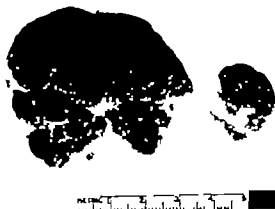


Fig. 1—Two excised sigmoidal polyps: the larger is the proximal lesion and the smaller the more distal one.



Fig. 2—The larger lesion: grade 1 adenocarcinoma in an adenomatous polyp (hematoxylin and eosin, X85).

Postoperatively the patient was entirely afebrile. In the first twenty-four hours after the operation the urinary output per rectal tube was 800 cc. and thereafter it ranged between 850 cc. and 1,800 cc. daily. Bowel movement of normal character and regularity were established by the eighth postoperative day. The patient resumed regular food

diet on the fifth postoperative day. At the time of dismissal from the hospital he was eating a full diet and colic function was normal. On the eighth postoperative day mild superficial wound infection developed and subsided within a few days of local treatment. Release from the hospital was on Feb. 1, 1954, at which time he was in good condition.

The patient reported by correspondence one month postoperative is that he was in splendid health, had regained his normal weight and is able to carry on his usual occupation and interests.



Fig. 3.—The smaller distal lesion: benign glandular structures in substance of the polyp and the surface covered with columnar epithelium (hematoxylin and eosin,  $\times 25$ ).

#### COMMENT

The presence of unilateral pyelonephritis, nonfunctioning kidney and polypoid sigmoidal lesions is of considerable interest and significance in this case. Renal complications of this nature are unfortunately a common early postoperative development. On the other hand, loss of function in previously normal kidneys many months or years after ureterosigmoidostomy occurs much less frequently. Few long-term studies are available to ascertain with any certainty the incidence of very late renal complications. A check of the record of cases at the Mayo Clinic revealed no instance of proved loss of function in an undiseased kidney after dismissal following ureterosigmoidostomy.

The history in this case suggests that the pathologic changes in the left kidney may have been due to repeated episodes of ureteral obstruction, pyelonephritis, or both for a period of five years. The anatomic proximity of both sigmoidal lesions to the respective ureteral orifices would strongly indicate that one or both could produce enough intermittent complete or partial obstruction to account for the renal disease. It is likely that the proximal sigmoidal polyp, since it was the larger, was present for a longer period of time and had produced its mechanical effects on that portion of the sigmoid involving the left ureteral opening. This is a probable explanation of why the left kidney showed the

evidence of disease. In the roentgenographic studies of the colon, the constricting defect suggestive of an infiltrating neoplasm, apparently represented a localized temporarily intussuscepted area produced by the large polypoid lesion below it. However there was no demonstrable pathologic process, as suggested by roentgenologic examination proximal to this large polyp on exploration. A localized recurring intussusception involving the segment of sigmoid where the left ureteral transplant was located is considered an important mechanical factor in producing intermittent left ureteral obstruction and eventual serious damage to the left kidney.

In spite of considerable anatomic involvement of the orifice of the right ureter by the distal colonic polyp there was, however, no evidence of significant amount of obstruction to the right ureter. There was no hydronephrosis on the right and the kidney felt normal, except for a slight congenital deformity in shape, to palpation at operation. It is interesting to speculate as to how much longer the right kidney and ureter would have remained normal.

The polyps which were seen in this case were similar to the adenomatous and carcinomatous polyps encountered in colons of many patients, with or without symptoms, and could not be distinguished histologically from the common solitary colonic or rectal polyps. It is of interest to note that the larger and probably the older contained region of grade 1 adenocarcinoma which, in our experience, are present in the great majority of these lesions. It is assumed, therefore, that these neoplastic lesions arose from the colonic mucosa and could be expected to behave as lesions of that origin.

In Hammer's case mentioned earlier the carcinoma present appeared to arise from the implanted remnant of vesical wall and was thought to originate near the orifice of the left ureter. Metastasis was not demonstrable. Death was due to uremia with hydronephrosis on the left and pyelonephritis on the right. A surgical treatment of the sigmoidal lesion was attempted. The author pointed out the marked predisposition of mucosa of ectrophied bladder to the development of adenocarcinoma and the histopathologic similarity of adenocarcinoma of colonic origin and adenocarcinoma primary in anomalous glandular structures in the urinary bladder. Hammer, however, believed that the cancer in his case arose from the implanted tissue and secondarily involved the wall of the near-by sigmoid. In our experience the epithelium of the ectrophied bladder will eventually undergo malignant change in a large majority if not all of the cases. If that epithelium is transplanted, it appears to retain this tendency.

The association of the intussuscepting large polypoid lesion near the colonic orifice of a transplanted left ureter with a severely damaged and infected left kidney occurring more than twenty-five years after successful ureterocolonic anastomosis, is of considerable importance and has been extremely instructive to us. It is seen, then, that colonic lesions may occur which could seriously impair a completely successful ureterocolonic anastomosis. In cases in which evidence of obstruction to one or both kidneys is present, particularly after many years have elapsed since the anastomosis, investigation of the distal port

rectal bleeding or intermittent lower abdominal pain related to bowel function, should strongly suggest the presence of a colonic lesion capable of obstructing an implanted ureter. Prompt treatment of the primary colonic lesion may allow satisfactory drainage of the upper part of the urinary tract and stop the destructive process in the kidney.

Transcolonic excision after transperitoneal sigmoidotomy is considered entirely adequate for the eradication of the type of polyps encountered in this case. Should more extensive carcinomatous involvement of the wall of the distal portion of the colon be suspected, a more radical attack would be in order. Resection of the portion of the bowel containing the ureteral anastomosis would obviously entail another ureterosigmoidostomy, a cutaneous ureterostomy or sacrifice of the kidney of the involved side. A colonic anastomosis would be required to remain unusually secure because of the urinary content of that segment of the large intestine. If reimplantation of the ureter into the colon is feasible, a site distal to the colocolostomy would be preferable. The anticipated risk of such extensive reconstructive procedures would be high. It would be useful to carry out this treatment in multiple stages, using a transverse complementary colostomy.

#### SUMMARY AND CONCLUSIONS

A case has been reported in which a patient was successfully treated by bilateral ureterosigmoidostomy and excision of the exstrophied bladder and returned thirty years later with an obstruction and infection of the upper left part of the urinary tract for which left nephrectomy was considered necessary. Examination of the colon revealed multiple polypoid lesions at or near the ureteral orifices, the one at the opening of the left ureter being the larger and undergoing early cancerous change. Transcolonic excision of both lesions was also performed and the patient made an uneventful recovery.

The circumstances encountered in this case have not, to our knowledge, been previously reported in the literature and represent a very unusual, but important late complication of ureterosigmoidal anastomosis.

Thorough proctoscopic and roentgenographic study of the distal portion of the colon should be made in cases in which, many years after successful ureterosigmoidal transplantation, evidence of obstruction of the upper part of the urinary tract develops. Successful eradication of the colonic lesions may relieve the obstruction of the upper part of the urinary tract and, along with treatment of the infection of the urinary tract, may eliminate the necessity of carrying out nephrectomy.

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### Erratum

In the November 1943, issue of the JOURNAL, page 806 the article, Surgical Management of Thoracic Duct Injuries, the titles following the authors names are interchanged. The address of Dr G B Hodge is Spartanburg, S C and the address of Dr Huxley Bridges now deceased, was Shreveport La.

# Editorial

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## Nitrogen Balance

WITHIN the past decade more and more attention has been given by surgeons to the nutritional deficiencies of surgical patients. It is now generally recognized that the patient whose nutritional deficiencies have been, in large part, corrected prior to operation will withstand the assault of anesthesia and operation better than one who is not so prepared. There remains, however, no unanimity of opinion regarding the methods best calculated to correct such deficiencies.

The study of the nutritional deficiencies in man has, in large part, centered around the protein imbalance which so many of these patients have suffered. It may well be that such intensive studies in a single direction have been correct, but all clinicians interested in this field must constantly remind themselves that nutritional deficiencies in man are usually of a complex nature.

One read that the metabolic needs of the patient have been met by the administration of 3 000 c.c. of a five per cent solution of glucose every twenty-four hours, an amount which provides but 600 calories a day approximately one-third of the energy requirements of a patient at rest in bed. Regardless of the statement that the total calories in the diet are not very important anyone who has studied the problem of undernutrition knows that the total caloric intake is important.

Time and again within the past five years, it has been stated that the protein requirement of the patient have been met because for short periods the patient has been in positive nitrogen balance. This statement may in reality mean very little for a positive nitrogen balance does not indicate positively that the nitrogen made available to the patient has been utilized to restore the depleted stores of tissue and plasma protein. Determinations of plasma protein concentration may mean very little under such circumstances, for these provide no concrete data which reflect the increase or decrease of the total plasma protein.

Certain of the substances being used to reinforce depleted protein stores are only slowly metabolized in the body following intravenous injection. Gelatin and serum albumin are conspicuous agents of this type and yet we are asked to believe that they too rapidly play a part in correcting a protein deficiency while in reality they are stored for relatively long periods in the body before they become available for utilization in a nutritional sense.

A positive nitrogen balance means only that more nitrogen has been retained in the body on a given intake than has been excreted. It should not be made to imply that deficiencies in a nutritional sense have been corrected. If we are to continue to utilize the tools of the biochemist we must learn how to use them and how properly to interpret the results, which our studies provide.

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### Erratum

In the November 1949, issue of the JOURNAL, page 803 the article, *Surgical Management of Thoracic Duct Injuries*, the cities following the three names are interchanged. The address of Dr. G. B. Hodge is Spartanburg, S. C. and the address of Dr. Hunter Bridges, now deceased, was Shreveport, La.

additional histologically proved cases of primary carcinoma of the liver have been placed on record. The various recorded series, with the 55 cases which form the basis of this report bring the number of histologically proved cases now on record to 1 616.

The 55 cases mentioned are all autopsied material. Six were located in the files of Touro Infirmary in New Orleans between 1937 and 1944 and 49 were found in the files of Charity Hospital of Louisiana at New Orleans between 1928 and 1944 the last year for which complete autopsy protocols are available in the record library at this time. In addition to a large number of cases classified in the Charity Hospital files as primary carcinoma of the liver on apparently sound clinical grounds, there have also been located at this institution 5 cases in which the diagnosis was made by inspection at exploratory laparotomy and 26 others in which it was made by biopsy under similar circumstances. 37 cases in which autopsy was performed but in which histologic examination was either not made or not recorded. 8 cases diagnosed by punch biopsy alone and, finally, 9 cases in which the diagnosis was made on the clinical picture and the finding of malignant cells in aspirated ascitic fluid. No instances in which diagnosis was made by examination of a resected specimen were located. The 98 cases in which diagnosis was made by other methods than complete autopsy are not included in this discussion and will be reported separately.

#### INCIDENCE

It is impossible to speak definitely concerning the incidence of primary carcinoma of the liver for two reasons. (1) In the absence of uniform diagnostic criteria, numerous reported cases must be viewed with skepticism, though clinically. In the cases discarded at the New Orleans Charity Hospital there is little doubt that most of them were actual instances of the disease. (2) Official statistical records are of no value because tumors of the gall bladder, bile ducts, and liver are grouped under a single heading.

*Race*—All the evidence indicates that primary carcinoma of the liver is most common in countries inhabited by the yellow-skinned and dark-skinned races. Composite autopsy reports from which regional incidences have been calculated (Table I) show that the disease is considerably more frequent in Asia and Africa than in Europe with the exception of Greece in which the frequency is greater than in Japan and China proper. The incidence in Italy (0 per cent) is also high in comparison with that of other European countries. The general incidence in Europe however is about the same as in America (0.20 to 0.6 per cent).

Report which can be broken down into their racial components indicate that the Chinese continue to show susceptibility to carcinoma of the liver even when they have changed their habitation. Hartz, writing from Curacao in the Netherlands West Indies, found 11 instances of carcinoma of the liver in 33 autopsies on Chinese subjects against only 4 instances in 130 autopsies on Negro and white subjects. Strong and Pitts<sup>26, 27</sup> in a study from the Vancouver General Hospital, found 10 cases in 139 autopsies on Chinese subjects

# Recent Advances in Surgery

EDITED BY ALFRED BLALOCK, M.D.

## PRIMARY CARCINOMA OF THE LIVER

AN ANALYSIS OF FIFTY-FIVE AUTOCHTHONOUS CASES, THE RECORD OF A CLINIC WITH  
RESECTION AND A REVIEW OF THE RECENT LITERATURE

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ALTHOUGH Rokitsansky distinguished between primary and secondary hepatic malignancy in 1849 it was not until 1876, when Kelsch and Krieger<sup>1</sup> reported two cases, that clinical detail began to be recorded. The lapse between the pathologic and the clinical recognition of the disease can be chiefly attributed to Virchow's insistence that sites commonly affected by secondary neoplasms were only rarely the sites of primary growths.

Certain other landmarks are important in the history of primary carcinoma of the liver. In 1888 Hanot and Gilbert<sup>2</sup> classified the disease on a gross pathologic basis into nodular carcinoma, massive carcinoma, and carcinoma with cirrhosis. In 1901 Eggel<sup>3</sup> improved on this classification by distinguishing a multiple nodular form, a solitary massive form, and a diffuse form. In 1911 Goldzieher and von Bokay<sup>4</sup> classified primary hepatic malignancies histologically as hepatocellular and cholangiocellular terms which are more precise than the nomenclature of hepatoma and cholangioma introduced by Yamigawa<sup>5</sup> in the same year. Later Ewing employed the term mixed tumor to indicate that both liver cell and bile duct cell carcinoma are present in the same neoplasm.

The surgical removal of a tumor of the liver was first attempted by Langenbuch<sup>6</sup> in 1888 and the first successful resection of a primary malignancy was accomplished by Lucke<sup>7</sup> in 1891. Keen,<sup>8</sup> in 1899 was apparently the first American surgeon to perform a successful resection.

Although primary carcinoma of the liver still presents many obscure and puzzling aspects, it can no longer be considered a rare neoplasm. When Eggel<sup>3</sup> reviewed the literature in 1901 only 163 cases had been recorded, and the validity of many of these was doubtful. By 1937 Charache<sup>9</sup> was able to collect 1125 cases, 16 of which were eliminated as duplicates by Warren<sup>10</sup> in 1944. Between Charache's report in 1939 and the present time (August 1945) 450<sup>11</sup>

— From the Tulane University School of Medicine, New Orleans, La.

additional histologically proved cases of primary carcinoma of the liver have been placed on record. The various recorded series, with the 55 cases which form the basis of this report bring the number of histologically proved cases now on record to 1 616.

The 5 cases mentioned are all autopsied material. Six were located in the files of Toussaint Infirmary in New Orleans between 1937 and 1944 and 49 were found in the files of Charity Hospital of Louisiana at New Orleans between 1928 and 1944 the last year for which complete autopsy protocols are available in the record library at this time. In addition to a large number of cases classified in the Charity Hospital files as primary carcinoma of the liver on apparently sound clinical grounds, there have also been located at this institution 2 cases in which the diagnosis was made by inspection at exploratory laparotomy and 96 others in which it was made by biopsy under similar circumstances. 37 cases in which autopsy was performed but in which histologic examination was either not made or not recorded. 8 cases diagnosed by punch biopsy alone and, finally, 2 cases in which the diagnosis was made on the clinical picture and the finding of malignant cells in aspirated ascitic fluid. No instances in which diagnosis was made by examination of a resected specimen were located. The 98 cases in which diagnosis was made by other methods than complete autopsy are not included in this discussion and will be reported separately.

#### INCIDENCE

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It is impossible to speak definitively concerning the incidence of primary carcinoma of the liver for two reasons. (1) In the absence of uniform diagnostic criteria, numerous reported cases must be viewed with skepticism, though clinically as in the cases discarded at the New Orleans Charity Hospital, there is little doubt that most of them were actual instances of the disease. (2) Official statistical records are of no value because tumors of the gall bladder, bile ducts, and liver are grouped under a single heading.

Race.—All the evidence indicates that primary carcinoma of the liver is most common in countries inhabited by the yellow-skinned and dark-skinned races. Composite autopsy reports from which regional incidences have been calculated (Table I) show that the disease is considerably more frequent in Asia and Africa than in Europe with the exception of Greece, in which the frequency is greater than in Japan and China proper. The incidence in Italy (0.4 per cent) is also high in comparison with that of other European countries. The general incidence in Europe however is about the same as in America (0.20 to 0.26 per cent).

Report which can be broken down into their racial component indicate that the Chinese continue to show a susceptibility to carcinoma of the liver even when they have changed their habitation. Hartz, writing from Curacao in the Netherlands West Indies, found 11 instances of carcinoma of the liver in 33 autopsies on Chinese subjects against only 4 instances in 1 300 autopsies on Negro and white subjects. Strong and Pitts, in a study from the Vancouver General Hospital, found 10 cases in 139 autopsies on Chinese subjects

TABLE 1. ADVERSE INCIDENCE OF PRIMARY CULICION OF THE LIVER IN VARIOUS REPORTED SURVEYS ON AMERICAN SERUM

PL. IN	NUMBER OF ADVERSE REACTIONS	NUMBER OF CLASSES (PER CENT)	PLACES	NUMBER OF ADVERSE REACTIONS	NUMBER OF CLASSES (PER CENT)
France 14	1,640	53	Paris, Antwerp	300	1
France, 14 in 602			Yverdon, 121	1,907	15
3 percent 8 in 1,118			Geneva 10 in 120		
Italy 14	9,231	109	White 2 in 1,825		
South Africa	4,964	61	San Francisco	11,043	49
Greece 14	3,029	41	Detroit, 23	3,437	15
Japan 14	42,975	431	St. Louis 14	2,800	16
China 14	21,478	184	Omaha 14	1,100	4
Netherlands West Indies	1,343	9	Buffalo, 17	7,400	28
China 3 in 23			Charleston 21	3,470	3
China 4 in 1,320			New Orleans	17,617	65
Italy 14, 15	42,065	216	New York 14	44,006	119
Philippines	12,516	61	Boston 14, 15	18,029	23
China 14	12,806	59	Baltimore, 20, 21	4,027	63
India 14	7,234	23	Washington, 14	10,017	20
Italy 14	6,000	18	Minneapolis	1,500	3
Switzerland 14	2,400	6	Richmond	16,203	21
East Asia 14	44,053	65	Chicago, 14	15,045	24
Holland 14	2,950	5	Lower City	5,100	1
Germany 14	17,715	231			
France 14					
Eastern	92,560	834	Various Elements		
Africa	4,861	61	America	180,709	478
Europe	274,417	546	Various	7,765	24
Central & South America	14,135	89			

<sup>a</sup> Bernhart's Collected Serology Project.  
<sup>b</sup> Calculated from the active listed above.

against 2 cases in 1,828 autopsies on white subjects. Wilbur and his associates<sup>20</sup> reported from San Francisco 19 instances of the disease in Chinese in a total of 49 autopsied cases. In view of the relatively small number of Chinese in America (77,504 out of a total population of 133,211,064, according to the 1940 census) the relatively large number of cases of primary carcinoma of the liver reported among them by Wilbur and his associates as well as by a number of other observers seems significant.

It is also possible that Negroes, when they leave their native habitat carry with them a predisposition to the disease, though the tendency is not as clear cut among them as it is among the Chinese. The disease is relatively frequent in Africa. Bergeret<sup>21</sup> who supplied no base figures, stated in a report from Dakar that primary carcinomas of the liver constituted 57 per cent of all carcinomas. Berman, who reported an incidence of 30 per cent for malignant disease in the general Bantu population, found that when the analysis was limited to carcinoma in adult male workers in the Witwatersrand gold mines whose ages ranged from 16 to 40 years, carcinoma of the liver comprised 90 per cent of the total number of cases. Primary hepatic malignancy has been reported to represent 18.7 per cent of all carcinomas in the semi Bantu races who inhabit the west coast of Africa.

Reports which emphasize the racial aspects of the disease are surprisingly few in America, and no studies have been reported from the South where, according to the 1940 census, the Negro population represented 4 per cent or more of the population in each of nine states. A compilation of reports from the United States, in which the racial components were clear revealed a composite autopsy incidence for primary carcinoma of the liver in Negroes of 0.44 per cent, which is somewhat higher than the incidence of 0.26 per cent calculated for the general population. According to Kinnaway<sup>22</sup> the available data supply no evidence that the American Negro is especially susceptible to the disease.

The Charity Hospital of New Orleans probably cares for the great majority of Negroes in Louisiana where colored persons comprise 35.9 per cent of the population. The autopsy figures, which can be broken down only after 1937 (Table II) reveal a smaller incidence of Negro than white although the Negroes slightly outnumbered the white people in hospital admissions between 1928 and 1944. The number of cases of primary carcinoma of the liver is, however, too small for much emphasis to be placed upon such calculations. The six cases reported from Toussaint Infirmary were all in white subjects, since that institution treats only white inpatients.

TABLE II. AUTOPSY INCIDENCE OF CARCINOMA OF THE LIVER. CHARITY HOSPITAL OF LOUISIANA IN NEW ORLEANS

TEGORIES	TOT	CASES	INCIDENCE OF LIVER	PROPORTION
Autopsies 1925 to 1944	13,737		49	0.35
Autopsies 1937 to 1944	760		46	0.26
White	2,674		1	0.45
Negro	4,096		14	0.34
Male	1,990		21	0.63
Female	770		6	0.18



*Sex*—The doubts occasionally expressed concerning the true racial incidence of primary carcinoma of the liver<sup>12</sup> do not exist concerning the sex incidence which is predominantly male. All reports bear this out. Berman's<sup>8</sup> figures for the Bantu races show the male-female ratio to be 7.1. Ninety-four per cent of Bergeret's 157 cases occurred in males. There was only one female in the 134 Chinese patients with the disease reported by Tull.<sup>13</sup> Twelve of Cunningham's<sup>22</sup> 14 patients were males, as were 47 of the 49 patients reported by Wilbur Wood, and Willett's<sup>19</sup> 14 of the 16 reported by Matthews.<sup>14</sup> 1 of the 14 reported by Loewen,<sup>17</sup> and 59 of the 67 reported by Gustafson.<sup>23</sup> All of Lynch's six (Negro) patients were males,<sup>15</sup> as were 51 of the 77 patients under 16 years of age reported by Steiner.<sup>16</sup>

The same male predominance is evident in the cases observed at the New Orleans Charity Hospital, where 36 of the 49 cases which make up the series occurred in males. Fourteen of the 22 white patients and 22 of the 27 Negro patients were males. Since the Negro female admissions were higher than the white female admissions, the disproportionately low incidence in Negro females may be significant. Five of the 6 cases analyzed at Toussaint Infirmary occurred in men.

*Age*—Primary carcinoma of the liver has been reported at all ages. The range in the 49 Charity Hospital cases was from 4½ months to 85 years, both the youngest and the oldest patient being white. The age distribution was about what would be expected for any malignant neoplasm: the greatest concentration of cases (36) occurring during and after middle life (between 41 and 70 years) but no age being immune. The most significant point concerning the age incidence is the apparent tendency of the disease to occur earlier in Negro than in white subjects. Seven of the 10 patients in the series who were under 40 years of age were Negroes. This tendency is in accord with the age incidence in other reports. In Berman's<sup>8</sup> study of the disease in the Bantu, for instance 82.6 per cent of the patients were under 40 years of age.

Primary carcinoma of the liver is relatively frequent in youth. Noeggerath<sup>24</sup> in 1854 observed a case in a newborn child, and Werdniger<sup>25</sup> reported a case in a 3-day-old child. Tomlinson and Wolff<sup>26</sup> in 1941 were able to collect 82 authentic cases in persons under 16 years of age. Eight cases in the same age group have since been reported in the literature.<sup>27-30</sup> and the addition of the 4 cases observed at Charity Hospital brings the total to 94.

*Sex and Age in Relation to Pathogenesis*—The predominance of primary carcinoma of the liver in the male sex has been explained as due to the higher incidence of cirrhosis of the liver while in the female the occurrence of the disease is explained by the frequency of intra-uterine infection.<sup>31</sup> The rather frequent statement that liver cell carcinoma tends to develop in the male and bile duct cell carcinoma in the female is not entirely borne out by the statistics. Eggel<sup>32</sup> found 5 per cent of the cholangiomas in his series in women, and 6 of the 11 cholangiomas reported by Hoyle and Kernohan<sup>33</sup> occurred in women, but only 2 of the 8 cholangiomas reported by Cunningham<sup>22</sup> occurred in women. In the Charity Hospital series 24 of the 29 cases of liver cell carcinoma occurred in males, as did also 9 of the 13 cases of bile duct cell carcinoma.

The statement is also frequently made that bile duct cell carcinoma occurs at a later age than liver cell carcinoma. The Charity Hospital series supports this observation. The age differential was particularly marked in colored patients, in whom the average age for liver cell carcinoma was 44.8 years, as compared with 58 years for bile duct cell carcinomas. In white subjects the difference was not significant.

#### ETIOLOGY

The etiology of primary carcinoma of the liver like the etiology of carcinoma in other locations, remains to be clarified, though certain factors seem to offer at least a partial explanation of its occurrence.

**Cirrhosis**—Of all presumably predisposing conditions, cirrhosis is most frequently incriminated, and the association is too striking to be explained away as merely coincidental, though it is impossible to determine accurately the number of cases of hepatic cirrhosis which are followed by primary hepatic malignancy. Various reports state the incidence to be from 9.8 to 54.5 per cent. Hepatic malignancy occurred in 90 or 45 per cent, of 1,989 cases of hepatic cirrhosis collected by Berk and Lieber, while in 1,073 cases of primary carcinoma of the liver collected by the same writers, cirrhosis was present in 638 or 61.3 per cent. In Berman's collected series the association was noted in 73 per cent of cases, while in his personal series it was noted in 79.6 per cent. Wilbur and his associates<sup>22</sup> found hepatic cirrhosis present in 76 of 49 cases of primary carcinoma of the liver. In the Charity Hospital Touro Infirmary series cirrhosis was present in more than 70 per cent of all cases (Table III) and was considerably more frequent in males than in females.

TABLE III. INCIDENCE OF CIRRHOSIS IN PRIMARY CARCINOMA OF THE LIVER IN RELATION TO THE TYPE OF MALIGNANCY AND THE SEX DISTRIBUTION

TYPE OF MALIGN	MALES		FEMALES		TOTAL		PERCENTAGE
	TOTAL	WITH CIRRHOSIS	TOTAL	WITH CIRRHOSIS	M OR FEMALE	WITH CIRRHOSIS	
Liver cell	4	3	8		20	7	62.5
Bile duct cell	9	3	4		13	5	38.4
Mixed cell	4		1	1	5	3	60.0
Undifferentiated	4	4	4		8	6	75.0
Total	21	14	17		38	25	65.8
Percentage	Males 67 per cent		Females 59 per cent		Total 74 per cent		

Cirrhosis is more likely to be associated with liver cell than with bile duct cell carcinoma. Gustafson<sup>23</sup> stated the respective incidences as 54.1 and 33.3 per cent. In Horne and Kohnan's<sup>24</sup> series cirrhosis was associated with 67 per cent of the liver cell carcinomas but with only 18 per cent of the cholangiomas. In our cases (Table III) cirrhosis was considerably more frequent in liver cell than in bile duct cell carcinomas.

Opinions differ as to the relationship between hepatic cirrhosis and primary carcinoma of the liver. In cirrhosis hyperplastic compensatory process occurs in perialveolar liver cells in response to a demand for increased functional activity<sup>25</sup> but whether some particular irritant or an actual carcinogenic factor

initiates a malignant change in the proliferative tissue is not yet known. Carle<sup>11</sup> believed that three possibilities must be considered: (1) Cirrhosis may precede the malignancy and play an etiologic role. (2) It may occur concomitantly as a result of the same irritative process responsible for the malignancy. (3) It may develop as the result of the neoplastic change. Still another possibility is that the underlying changes in hepatic cirrhosis, which are an increase in connective tissue associated with damage to and loss of liver cells, serve merely as an important prerequisite for carcinomatous change. Whatever the train of events, the association, as has been pointed out, is frequent and it is sometimes extremely striking as in the case reported by Mensch and Hanno<sup>12</sup> in which cirrhosis was known to have been present for eight years before carcinomatous changes were observed in the liver with metastases to the osseous system.

Laennec's (portal) cirrhosis is the type of cirrhosis usually associated with primary carcinoma of the liver. When hemochromatosis is present, the cirrhosis is usually of the pigmentary type. yellow atrophy cirrhosis (Biliary toxic cirrhosis) is only occasionally observed.<sup>13, 14</sup> Some observers<sup>15</sup> consider that the role of the latter varieties is of more importance in the etiology of primary carcinoma of the liver than the role of portal cirrhosis.

Willis<sup>16</sup> was of the opinion that in hemochromatosis the liver is inherently cancerous. primary hepatic carcinoma was present in three of his seven cases of hemochromatosis, and Berk and Lieber<sup>17</sup> who found the association in 3 of 15 cases, were of the same opinion. Hemochromatosis was present in all 6 cases of primary carcinoma of the liver reported by Laneh,<sup>18</sup> all of which occurred in the Negro. Stewart<sup>19</sup> on the other hand, found the two diseases associated in only 14 of 190 cases (11.6 per cent) while Sheldon<sup>20</sup> thought that the association was at the most not more than 6 or 7 per cent, and concluded that primary carcinoma of the liver was more apt to occur in organs which were the site of hemochromatosis than in those in which the more usual nonpigmentary variety of cirrhosis was present. In 436 collected cases of hemochromatosis there were 37 cases of primary carcinoma of the liver or 3 per cent, which seems to support Sheldon's point of view.

**Alcohol.**—The possible relationship between alcohol and cirrhosis of the liver is no part of this discussion, though it should be remembered that it may exist. Some investigators,<sup>21</sup> however have suggested that alcohol especially among the more primitive races, may play some part in the production of hepatic malignancy by supplying sufficient irritative and noxious influences to produce carcinomatous changes in a cirrhotic liver. The alcohol imbibed from an early age by certain Bantu in Africa is particularly powerful, and the speculation seems warranted that some relationship may exist between the noxious effects of alcohol consumed by primitive races and the high incidence of primary hepatic malignancy among the young people of those areas. A definite history of alcoholism was obtained in 10 of the 50 patients in the Charity Hospital-Touro Infirmary series.

**Chronic Irritation.**—Chronic irritation is known to be an important etiologic factor in the production of carcinoma in certain organs of the body. Cholelithiasis, for instance, is present in most cases of carcinoma of the gall bladder.

The same reasoning has been applied to the etiology of primary hepatic carcinoma. Sanes and MacCallum<sup>1</sup> reported two cases of hepatolithiasis associated with carcinoma of the intrahepatic bile ducts, and Armanino<sup>2</sup> reported a case of carcinoma of the liver in a 17 year-old boy in which it was thought that the carcinomatous changes were initiated by the presence of a choledochus cyst and the resulting changes in the biliary tract and the liver. Pomeranz and his associates<sup>3</sup> also advanced the theory that chronic infection of the gall bladder with cholelithiasis may contribute to the production of adenocarcinoma of the intrahepatic bile ducts.

*Parasites.*—Parasitic infestations of the liver have been suggested as etiologic factors in primary carcinoma of the liver on the ground that they cause hepatic irritation and damage. All the parasites which may infest the liver have been implicated at various times.<sup>4, 5</sup> That parasites play a part in the production of cirrhosis seems reasonable, but even in parts of the world in which both hepatic parasitic infestations and primary hepatic carcinoma of the liver have their greatest incidence a true cause and effect relationship remains to be demonstrated.

*Syphilis.*—Spirochetal infection has been mentioned as a possible etiologic factor in primary carcinoma of the liver<sup>6</sup> and there is no doubt that syphilis may play a part in the production of an antecedent cirrhosis. Moreover syphilis and hepatic malignancy are frequently associated, especially in dark skinned races. Syphilitic lesions of the liver are however seldom found at autopsy. In the 55 cases which make up the present series, the blood serology was positive only 6 times, and too much significance must not be attached to those cases, since false-positive reactions are fairly frequent in carcinoma of the liver.

*Congenital and Hereditary Factors.*—Stiles<sup>12</sup> work has clearly shown that in mice hereditary factors are responsible for the production of hepatic neoplasms. No such proof exists for the development of the disease in human subjects, although in some of the more frequently affected races a hepatic tumor diathesis has been postulated, analogous to the genetic constitution which predetermines the incidence of carcinoma in certain strains of rats.

Pepere<sup>13</sup> has suggested that all solitary adenomas of the liver are congenital, and congenital malignant adenomas have been described by Ewing<sup>14</sup> and by Ribbert<sup>15</sup> and others. Strong support has been given to the thesis that in the newborn infant and in young children, neoplastic changes readily occur as a result of congenital maladjustment of liver cells.<sup>16</sup> Cirrhosis is seldom seen in association with primary carcinoma of the liver in patients under 16 years of age, as Steiner<sup>17</sup> has pointed out and Mudgett and associates<sup>18</sup> have also advanced the opinion that teratoid carcinomatous growths in very young children can best be explained on a purely congenital basis. Muir maintained that hepatic adenomas undergoing malignant changes often arise from displaced cells, but adequate proof remains to be adduced. Teratomas, from which hepatic cancers may arise are known to result from developmental abnormalities. It is doubtful that congenital maladjustment of liver cells with a predisposition to cancer formation explains many cases of primary carcinoma of the liver in

adults, but the explanation, as has been contended, may be of much more significance in youth.

**TRAUMA.**—Crawford, among other writers, has cited cases of primary carcinoma of the liver in which trauma was thought to be a possible etiologic factor; in fact the malignancy was believed to have been precipitated by an abdominal injury. The possibility cannot be entirely discounted, but the number of cases in which the association existed is still small and the element of pure coincidence must be kept in mind.

**Dietary and Nutritional Factors.**—Probably the most important advances in the investigation of the etiology of primary carcinoma of the liver concern possible nutritional factors. It seems something more than coincidence that the greatest incidence of the disease is in those countries and among those races in which the diet is poorly balanced and generally inadequate. Among the Bantu of South Africa, where as has been pointed out earlier in this paper primary carcinoma of the liver is a frequent disease, hepatic cirrhosis is observed in approximately four of every five patients who come to autopsy. The staple diet of this race consists chiefly of corn meal and fermented milk. Meat is a luxury which is only occasionally possible. The diet is therefore high in fat, low in protein, and extremely deficient in vitamins (Gilbert and Gillman).<sup>44</sup> Those who fed this staple diet to young rats, were able to produce marked fatty changes in the liver with associated cirrhosis. Hepatic neoplasms have also been observed in experimental animals fed for long periods of time on diets which favor the development of cirrhosis.

The evidence strongly suggests, as Ruch and Brumann<sup>45</sup> saw it, not that cancer is the result of a deficient diet or that certain diets induce the development of cancer—since neoplastic development and growth depend on many factors—but rather that primary carcinoma of the liver may be frequent in peoples of Asia and Africa because their diets are lacking in certain factors essential for a defense mechanism against malignancy. Whatever the relationship, hepatic cirrhosis, hepatic malignancy, and the elements of the diet seem closely associated, and the diet is perhaps of most importance according to evidence now available that any other recognized contributory factor.

**Experimental Evidence.**—An extended discussion of the experimental production of cancer is beyond the scope of this communication, but certain studies related to primary carcinoma of the liver must be briefly mentioned.

Most important of the chemical agents now under investigation are the aromatic compounds, notably O-amino-azotoluene and 1-dimethyl-amino-azobenzene. If these agents are incorporated in the diet fed to rats and mice, well-marked cirrhosis develops, which may progress to cancer formation.<sup>46, 47</sup> If however the same diet is fortified with a large quantity of protein and vitamin B complex, the development of hepatic carcinoma is greatly delayed. If the diet is kept deficient in these elements, the rate of cancer formation is increased. The evidence thus suggests that adequate dietary elements may protect the liver cells against carcinogenic agents. The effects of 2-ethylamino-fluorene are similar to those of dimethyl-amino-azobenzene. It is more difficult, however, as

Bielchowsky showed, to inhibit carcinogenesis in rats by an adequate diet when the former agent is used.

The malignant changes produced by carcinogenic agents occur subsequent to cirrhotic changes, though the evidence suggests that cirrhosis is not an essential precursor.<sup>26</sup> On the other hand, as Orr<sup>27</sup> demonstrated, the yield of malignant tumors is greater when it occurs.

Considerable attention has been devoted to the effect of diet on artificially produced hepatic malignancy. Opie<sup>28</sup> demonstrated that rice actively factors carcinogenesis, while Sugimura and Rhoads<sup>29</sup> showed that cirrhosis and cancer produced by dimethyl-amino-azobenzene could be completely inhibited if 15 per cent of the diet consisted of fat. Opie showed that the appearance of hepatic carcinoma in experimental animals was greatly accelerated by a fatty diet of low protein content and White and Edwards<sup>30</sup> made the same observations in connection with alanine and methionine. Sugimura obtained partial inhibition of malignant hepatic tumors by the use of dried whole milk, with which he also reported the successful treatment of cirrhosis. Riboflavin has been shown to have an inhibitory effect on carcinogenesis.

Dietary inclusion and deficiencies do not affect all artificially produced hepatic neoplasms in the same manner. Thus tumors induced by *N*-acetylamine fluorene were not influenced by variations in the protein content while those produced by dimethyl-amino-azobenzene were definitely affected.<sup>31</sup>

*Intrahepatic Carcinogenic Factors*.—Several writers, among them Schachel,<sup>32</sup> Des Ligneris,<sup>33</sup> Hueber,<sup>34</sup> Steiner<sup>35</sup> and Hannum<sup>36</sup> have suggested the existence of a carcinogenic factor in the human liver. According to Steiner and Des Ligneris this factor is present in apparently normal persons as well as in those with carcinoma somewhere in the body. Des Ligneris, whose studies were conducted among Bantu, showed that this presumptive factor is present to a greater degree in this race than in the white race though according to Steiner<sup>35</sup> it is no more common in the American Negro than in white subjects. These facts raise the question whether the difference between the American and the African Negro is on a constitutional or on an environmental basis. In Steiner's<sup>35</sup> opinion the carcinogen is present in the Bantu as the result of environment and not because of any racial disorder of metabolism.

#### CLINICAL PICTURE

The statement is frequently made that the clinical course of carcinoma of the liver is not characteristic and that the clinical characteristics of the disease differ from case to case. The statement is not precisely correct. The rapidly fatal course of event is unfortunately all too characteristic. Furthermore certain symptoms and signs appear in combination fairly frequently though it must be granted that they are in no sense pathognomonic either individually or collectively. Clinical classification has however been worked out by Bertram Fung<sup>37</sup> and Gustafson<sup>38</sup> and a comparison of important reported series with the series reported in this communication (Table IV) indicates that certain clinical findings tend to be prominent in many cases.

*Symptom*.—Abdominal pain, which was present in 37 cases, was the most important symptom in this series, as it is in all reported series (Table IV) and

was likely to be the first symptom noted by the patient. In this series it was the first symptom in 96 cases. It was usually situated in the epigastrium and right hypochondrium and was usually of a dull, persistent character never being severe enough in itself to force the patient to seek immediate medical attention. A history of acute attacks of severe pain was seldom present, even in association with hematemesis, which was entirely painless in 4 of the 6 cases in which it was observed. Severe pain, in contrast, was experienced in the cases of intraperitoneal hemorrhage, which variously occurred as the result of a breakdown of, or hemorrhage into a subcapsular nodule, or as the result of rupture of esophageal varices into the peritoneal cavity.

TABLE IV. COMPARATIVE DISTRIBUTION OF CLINICAL FINDINGS IN VARIOUS REPORTED SERIES OF PRIMARY CARCINOMA OF THE LIVER

CLINICAL FINDINGS	NEW ORLEANS (55 CASES) (PER CENT)	MAYO CLINIC (31 CASES) (PER CENT)	LA FAYETTE (47 CASES) (PER CENT)	CYCLES ET AL. (37 CASES) (PER CENT)	COLLECTED SERIES (500 CASES) (PER CENT)
Abdominal pain	47	27	72	71	23
Distention	53	37			
Weight loss	4	71			
Weakness	23	37	57	91	23
Nausea, vomiting	15	45		44	12
Jaundice	44	58	67	89	24
pedal edema	44	74	4	46	40
Dyspnea	44				
Hepatomegaly	84				
Palpable mass	23	64.1	77	91	69
Hepatic tenderness	27			13	17
Fever	46	29		75	24
Ascites	54	77	60	37	44
Dilated abdominal veins	23	29			
Splenomegaly	5	19			
Anemia	31		23	87	64
Gastrointestinal bleeding	11		14		
Pulmonary signs	31				
Delirium, coma	18				

In 5 instances the pain was described as indigestion and was thought to bear some relationship to the ingestion of food, though as a rule pain and digestive disturbances were not related. Pain in the scapular regions, the back, and the lumbosacral region was complained of by 8 patients, in 4 of whom it was the first symptom. Abdominal pain was not present in any of these cases.

Abdominal distention was complained of by 46 patients, in 4 of whom it was the first symptom. It was usually of gradual and insidious onset. Twenty-four patients, 16 of whom were Negroes, complained of dyspnea, which was the first symptom in 8 cases. This is apparently a more important symptom than the literature would suggest. It was associated with ascites in 13 cases, but the association obviously does not explain all cases.

Loss of weight was complained of during the course of the disease by 43 patients, but was the first symptom in only 5. The average weight loss was between ten and twenty five pounds, but losses of as much as forty pounds were recorded. Emaciation, however, was more likely to be a terminal than an

initial finding. Asthenia, malaise, and anorexia though they are often stated to be major symptoms in carcinoma of the liver occurred in only 19 of the 65 cases in this series and were the first symptoms in only 4.

Nausea and vomiting occurred during the course of the illness in 19 patients but were the first symptoms in only 3. Frank hematemesis occurred in 6 cases, in all of which it was a terminal fatal event. In only one other case was the vomitus described as bloody or of the coffee-grounds variety. Diarrhea was complained of by 9 patients and constipation by 4 but in no instance was either a first symptom.

Jaundice was present in 11 patients, only 3 of whom were Negroes, but was reported as a first symptom by only 4. It is not unusual, of course, for jaundice to be overlooked by Negro patients and by their families, or for that matter by dark skinned white patients. It was eventually present in 4 cases in the series, but was usually a terminal or at least a late sign.

Swelling of the feet was complained of by 17 patients, 6 of whom listed it as a first symptom, but on examination it was found to be present in 7 other patients. It was bilateral in all instances. In 4 cases the edema extended from the feet into the scrotum.

Delirium, without excitement but passing into coma, occurred in 10 patients as a terminal event from which none recovered. In one case coma was associated with hemiplegia and led to a diagnosis of cerebral vascular accident but autopsy revealed nothing pathologic in the cerebrum. In one case reported by Zeller and Mallory<sup>21</sup> the patient presented a positive Babinski sign and spastic, followed by flaccid paralysis, but at autopsy no pathologic process could be demonstrated in the central nervous system. The authors pointed out that symptoms referable to the central nervous system which often are quite marked, may accompany hepatic insufficiency. The clinical picture is analogous to that observed in uremia, in which symptoms referable to the central nervous system are prominent clinically but in which only minimal nonspecific lesions are found in the brain at autopsy.

Earlier studies of carcinoma of the liver indicate that fever is common in this disease. This was not true in the Charity Hospital-Touro Infirmary series. It was noted in 77 cases, in 10 of which it was a first symptom, but it was usually a terminal event which followed a characteristic pattern, the temperature rising from a previously normal level in a sudden steplike elevation which heralded the approaching exodus. Terminal rises of 105 and 106° F. were not uncommon, but temperature elevations, if they were present earlier in the course of the illness, were intermittent and seldom exceeded 101 or 102° F. The septic type of temperature which was occasionally observed could usually be explained by the finding at autopsy of central hepatic necrosis often associated with cavity formation.

*Physical Findings*—By far the commonest finding on physical examination in the Charity Hospital-Touro Infirmary series was enlargement of the liver which was noted in 46 patients, although tenderness was associated in only 18 cases. The enlargement amounted to only 3 cm. in some cases, but in



others the liver extended down into the pelvis. The hepatic enlargement was sometimes not apparent on the first examination because of the presence of ascites, which was readily demonstrable on physical examination in 30 cases. After paracentesis the edge of the liver could not infrequently be palpated considerably below the umbilicus.

Although its surface was frequently described as nodular a definite mass arising from the liver was noted in only 15 cases, in 2 of which the finding of the mass was the first evidence of illness. Dilated abdominal veins were present in 14 cases; usually they appeared only above the umbilicus and often they extended up into the chest. Small telangiectatic areas were occasionally noted on the back or in the scapular regions.

Signs of pulmonary involvement ranging from coarse rales to massive consolidation, were noted in 17 cases. The findings were highly suggestive of metastases, but definite evidence on this point could not be established in any case merely by physical examination. In 9 cases it was possible to demonstrate a raised, fixed lobe on the right side of the diaphragm, this number not including upward enlargements of the liver in which the diaphragm was not fixed.

The spleen was palpable in 3 cases, and in 8 other cases purpuric manifestations were present in the form of small petechial cutaneous hemorrhages.

#### PATHOLOGIC PROCESSES

Macroscopically it is not possible to distinguish between liver cell and bile duct cell carcinoma; the final diagnosis always resting with the pathologist. It was possible, however, on gross examination to divide 51 of the 55 cases into three pathologic groups: (1) local massive carcinoma, (2) local nodular carcinoma, and (3) diffuse nodular carcinoma. In some instances local massive carcinoma appeared in combination with one or the other of the nodular types, most often the diffuse nodular type.

The liver was found to be greatly enlarged on gross inspection at autopsy in 40 cases. The average weight was 2,200 Gm. but the range was from 1,200 to 7,000 Gm. Often the enlargement was extremely irregular. One of the lobes, most often the right, was likely to be greatly enlarged while the left and caudate lobes were small. In all instances massive enlargement of a single lobe could be accounted for by the presence of local massive carcinoma. The largest livers, however, were the sites of diffuse nodular neoplasm, the numerous nodules of which had replaced most of the normal liver tissue.

*Local Massive Carcinoma*.—Local massive carcinoma, in which a single large nodule was present in one lobe or in which a multitude of smaller nodules had coalesced to form a large nodule, was found in twelve cases. In nine instances a single large nodule was present, usually in the right lobe; in the remaining cases local nodules were also present. In some cases the entire right lobe had been replaced by a massive carcinoma derived from the confluence of smaller nodules.

The consistency of the tumor masses depended upon the amount of secondary change which had occurred. Sometimes they were firm frequently

they were quite soft because of the presence of liquefied matter. In this type of carcinoma necrosis was frequent and hemorrhage into the nodule not uncommon. Often a cavity filled with yellow cheesy, sometimes bloodstreaked material suggested a possible liver abscess. Berman was of the opinion that tumors of soft consistency were of the rapidly growing type. Necrosis in nodules near the surface of the liver was frequently associated with adhesions between the diaphragm and the hepatic capsule and the omentum, stomach, and intestines, were also often adherent to the liver.

*Local Nodular Carcinoma*—Local nodular carcinoma in which two or more nodules were present in a circumscribed area, was found in six cases, in three of which the nodules were found in association with massive carcinoma. In all three cases the local growth was present in one lobe of the liver and the massive growth in another. It is a rule a few nodules, ranging in size from a pea to a pigeon's egg, occurred close to each other in a single area of the liver. Sometimes Gibson's capsule was raised by nodules near the periphery and small irregular bosses could be palpated. In other instances the surface of the liver was smooth and palpation furnished no intimation of the serious disease process present within the substance of the organ. On section the nodules were usually found to be fairly firm and whitish gray. They were often bile-stained but were seldom hemorrhagic. Secondary changes were also infrequent.

It is quite possible that local nodular carcinoma represents simply an intermediate process between a single local malignant nodule and the diffuse nodular variety of the disease. The local nodules may eventually coalesce to form a single massive tumor or may metastasize within the liver and present as a generalized nodularity.

*Diffuse Nodular Carcinoma*—Diffuse nodular carcinoma was present in 33 cases, in 15 of which it was associated with massive carcinoma. The liver was often bizarre in shape, one or two lobes, the entire organ being riddled with innumerable nodules of all sizes, shapes, color and consistency. The smaller nodules tended to be located toward the periphery, though small nodules were often found encircling larger nodules in the depths of the hepatic substance. Larger nodules were likely to be necrotic and often consisted of little more than a shell. Smaller nodules were likely to be hard and gritty.

Hemorrhage was frequent in this type of case as was hemoperitoneum as the result of rupture of necrotic nodules near the surface of the liver. In a number of cases differentiation between the nodular and the massive form of carcinoma was difficult, for coalescence of nodules appeared to give rise to several massive tumors. Whether the massive form developed first and gave rise to secondary nodules or whether the nodules appeared first and coalesced to form the massive type of neoplasm is open to speculation.

#### HISTOPATHOLOGY

*Luteal Cell Carcinoma*—Carcinoma arising from luteal cell in this series conformed, in general, to the structure of normal hepatic architecture. The tumor cells were large, ranging in size from 10 to 20 microns and were polygonal

They were arranged in cords or trabeculae usually to a thickness of two to ten cells, separated from each other by a very fine stroma with abundant vascular elements. These sheets of cells sent fingerlike projections into normal liver tissue and surrounding connective tissue. Scattered nests of irregularly arranged cords were not uncommon.

The cells frequently had large round hyperchromatic nuclei. Often the nucleus practically filled the cell, leaving only a fine ring of cytoplasm at the periphery. It was often vesicular and finely granular and a well-marked chromatic network was visible. Nucleoli were usually seen.

The cytoplasm of the neoplastic cells was characteristically granular and either fine or coarse. Bile pigment was often seen within the cytoplasm, which was occasionally described as foamy. Not infrequently cells with vacuolated cytoplasm could be seen in areas farthest from the blood supply. Mitotic figures were extremely common, while giant cells, some with as many as ten to fifteen nuclei, abounded in the area of the neoplastic cells.

Necrosis, hemorrhage and hyaline degeneration were frequent. Normal liver cells near areas of neoplastic cells were small and granular and often showed marked fatty degeneration. In some cases in this series they were compressed by rapidly growing malignant cells, so that their shape was bizarre and they presented pressure atrophy and necrosis. In some areas an attempt at cell regeneration was observed, with both tumor cells and hyperplastic liver cells present in the same lobule. Regeneration of cells was frequently striking, the new liver cell usually being arranged in the form of small nodules surrounded by fine strands of periportal fibrous tissue. The stroma between the cord of tumor cells was of the finely avascular type. It became coarser toward the periphery and eventually took the form of cirrhotic strands surrounding the tumor nodules. Newly formed blood vessels were abundant and attempts at bile duct formation were frequent. Free tumor thrombi were frequently observed within the lumina of blood vessels and sinusoids.

Round cell infiltration, which was common, was particularly frequent in tumors associated with fairly well marked portal cirrhosis. Polymorphonuclear leucocyte infiltration was occasionally observed.

*(Cholangiocellular Carcinoma)*—In cholangiocellular carcinomas the histologic picture was characterized by groups of cells aggregated into definite alveolar or acinar formation, sometimes tending to form pseudoglands. The cells were usually columnar but were often of the cuboidal epithelial type although irregular shapes were not uncommon. The nuclei, which were markedly hyperchromatic, were usually situated at the base. The cytoplasm was clear. Mitotic figures were seldom seen, though mitosis was much more frequent in cases in which wild disorderly growth occurred in dense connective tissue toward the periphery of a nodule. Giant cells were also not often seen.

In contrast to the liver cell type of hepatic malignancy a vascularity of the stroma was the prominent feature in cholangiocellular carcinoma. The connective tissue consisted of dense thick cords, with very few blood vessels. Newly formed bile ducts were present in moderate numbers. Lymphocytic infiltration into the connective tissue was occasionally observed.

*Mixed Cell Carcinoma*—In five cases histologic examination showed characteristic features of liver cell and bile duct cell carcinoma in the same growth. Herxheimer<sup>22</sup> and Fischer<sup>23</sup> advanced the hypothesis that bile duct cells are transformed into liver cells in neoplasms originating from bile duct cells. Muir<sup>24</sup> and Rolleston<sup>25</sup> took the opposite position and traced bile duct cell formation from liver cells. Many authors,<sup>22, 23, 26</sup> considered that some tumors might be of dual origin and presented both varieties of cells. Whatever their origin, these cholangiohepatomas, to use Warria's<sup>24</sup> nomenclature or mixed tumors, to use Ewing's,<sup>27</sup> are apparently not common.

*Histogenesis*—Up to this time the origin of hepatic carcinoma has not been established. Advocates of the multicentric theory contend that numerous primary foci of liver cell cancer can arise simultaneously or in succession in the same liver by the transition of hyperplastic liver cells into malignant cells, and that a similar metamorphosis occurs in bile duct cells. Advocates of the unicentric theory on the other hand, contend that there is but one primary nodule and that all secondary nodules arise from it by simple intrahepatic metastasis, spread being accomplished by early invasion of the portal blood vessels. On the surface, the latter theory seems the more reasonable.

#### METASTASES

Extrahepatic metastases according to Greene,<sup>28</sup> Charache<sup>29</sup> and others, are relatively infrequent in primary carcinoma of the liver and considerably less frequent than in carcinomas elsewhere in the body. The series reported in this communication does not bear out these opinions. In 40 of the 50 cases, 79.7 per cent, clear-cut evidence of spread beyond the liver was found at autopsy (Table V). Metastatic lesions to the number of 120 were found in 22 different sites. Ewing,<sup>27</sup> in line with the opinion expressed by Liza and Hart<sup>30</sup> that liver cell carcinomas tend to metastasize via the blood stream and bile duct cell carcinomas via lymphatic channels, stated that hepatomas metastasize more often than cholangiomas. In this series, 23 of 29 hepatomas had metastasized beyond the liver as had 9 of 13 cholangiomas, of 5 mixed tumors, and 8 of the 8 tumors in which histologic differentiation was impossible. Metastases from hepatomas numbered 79 and were found in 19 different sites. Metastases from cholangiomas numbered 22 and were found in 8 different sites. Metastases from tumors of undifferentiated cell types numbered 19 and were found in 22 different sites, and metastases from mixed cell tumors numbered 7 and were found in 6 different sites.

Metastases to the regional lymph nodes (porta hepatis, mediastinal, mesenteric, gastrophatic periaortic and retroperitoneal lymph nodes) and to the lungs were most frequent. The right lung was more often affected than the left. Pulmonary metastases would be expected, since carcinoma of the liver can spread by way of the blood and the lymph stream as well as extend directly through the diaphragm and spread by contiguity. In a few cases a bloody pleural effusion was observed on the right side, in the absence of metastases in the pleura or the lung. Mallory<sup>31</sup> who reported similar observations, expressed

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In contrast to the liver cell type of hepatic malignancy a avascular stroma was the prominent feature of cholangiocellular carcinoma. The connective tissue consisted of dense thick cords with very few blood vessels. Very little lymphocytic infiltration

Bony metastases occurred in three cases twice to the ribs and once to the thoracic vertebra. In one instance the skin over the lower right costochondral junction was the site of metastasis. There was no instance in this series of the type of metastasis in which a Horner's syndrome is produced by the presence of secondary nodules in the lowest cervical vertebra and the sympathetic ganglion. In a case of this sort described by Cabot the clinical picture simulated that associated with Pancoast's tumor as the result of a large metastatic nodule in the apex of the lung.

Metastatic nodules in both bones and lungs have frequently been reported to show bony formation.<sup>22</sup> This phenomenon was observed in some pulmonary metastases in this series but not in any instance of osseous metastasis.

Malignant thrombi were present in the veins in several cases in this series. They were present in the hepatic vein in ten cases, in many of which histologic examination of sections of the vein showed that the presumed thrombi were actually metastases to the venous wall.

The portal vein contained malignant thrombi in seven cases, in each of which ascitic fluid was present though it was bloody in only two instances. Gelfand<sup>24</sup> considered that portal thrombosis explained the presence of bloody or serosanguineous ascitic fluid in primary carcinoma of the liver though as this series demonstrates, the ascitic fluid is not necessarily bloody when portal thrombosis is present. According to Mallory<sup>25</sup> hypernephroma involving the renal vein and the vena cava is the only neoplasm in addition to hepatoma which ordinarily extends into the veins in the form of gross thrombi.

In two of the seven cases in this series in which thrombi were found in the inferior vena cava large thrombi were also found in the right auricle definitely attached to areas of infiltration in the auricular wall. Simpson,<sup>26</sup> Gregory<sup>27</sup> and Rowen and Mallory<sup>28</sup> have all pointed out that such an association is extremely infrequent. According to Gregory<sup>27</sup> thrombi in the inferior vena cava should be suspected if dilated superficial veins are present in the antero-lateral portion of the thorax and the abdomen; their presence in this location was noted in five of the seven cases of inferior vena cava metastases in this series. In only one instance however was pain in the back associated with a thrombus in the inferior vena cava; this association was first pointed out by Pleasants<sup>29</sup> in 1911. Clinically severe dyspnea, jugular engorgement, and a sudden increase in the amount of ascites are often associated with thrombosis of the inferior vena cava with extension to the right auricle though no such association was observed in this series.

#### COMPLICATIONS AND COINCIDENT DISEASE

Hemorrhage is the most serious complication of primary carcinoma of the liver. Sometimes it takes the form of a slow ooze from an area in the periphery of the organ. At other times it occurs as a massive fatal loss of blood, the clinical manifestations of which suggest an acute abdominal condition (Beckman's acute abdominal cancer). Numerous instances are reported in the literature though the Charity Hospital-Touro Infirmary series contain none.

TABLE V DISTRIBUTION OF METASTASES IN PRIMARY CARCINOMA OF THE LIVER

SITES	NUMBER OF CASES WITH METASTASES	PROPORTION OF ALL (40) CASES WITH METASTASES
Lymph nodes	27	67.5
Thoracic		
Lungs	27	67.5
Diaphragm	8	1.5
Pleura	3	7.5
Intra-abdominal		
Omentum	6	15.0
Peritoneum	5	12.5
Intestinal wall	4	10.0
Gall bladder	3	7.5
Adrenal glands	2	5.0
Kidney	2	5.0
Cul-de-sac	1	2.5
Pancreas	1	2.5
Mesentery	1	2.5
Spleen	1	2.5
Extra-abdominal		
Hepatic vein	10	25.0
Portal vein	7	17.5
Inferior vena cava	7	17.5
Right atrium	2	5.0
Bones		
Ribs		5.0
Vertebrae	1	2.5
Abdominal wall		
Anterior	1	2.5
Posterior	1	2.5
Skin	1	2.5

the opinion that a fairly free passage of fluid could take place to the right pleural cavity through the diaphragm. In one of the three instances of pleural metastases no secondary nodules were found in the lung.

It is rather surprising that metastases were not more often present in the omentum (Table V) for in many cases it was adherent to the liver in the region of large necrotic nodules, especially in instances of local massive carcinoma with necrosis. Generalized peritoneal seeding was observed in only one of the five cases in which peritoneal metastasis had occurred. In two of the three cases in which the intestinal wall was infiltrated the spread could be explained by direct extension, because the hepatic flexure in one instance and the jejunum in the other were attached to the liver by adhesions in the region of necrotic nodules.

Secondary nodules were present in the cul-de-sac twice; their presence in each instance probably being due to cancer cells which had dropped from liver nodules into the pouch. In one of these cases the peritoneum and omentum were the site of metastases, but in the other no intra-abdominal secondary nodules could be identified. The spleen was affected in only one case which does not seem to bear out Liber and Brown's suggestion of a possible lymphatic spread from the liver to the spleen.

In all five cases in which metastases were found in the diaphragm the extension was presumably direct, the diaphragm being adherent to the liver in the region of malignant nodules. It is surprising that this structure like the omentum is not more often the site of metastatic growths.

lowered, though the albumin-globulin ratio was rather frequently reversed. Icteric indices are usually not very high, even when frank jaundice is present. The highest reading in this series was 150. If pathologic bone conditions can be excluded, an elevated alkaline phosphatase is suggestive of obstructive disease of the liver. In Gutman's<sup>24</sup> studies with this test primary carcinoma of the liver was always associated with values of more than 10 Bodansky unit.

Tests of liver function should be carried out in all cases but should be interpreted with caution for the physiologic properties of the liver are such that it can be extensively invaded by a malignant growth or other disease processes while the functional values remain normal or close to normal. If this possibility is borne in mind, information of value may be secured from tests of prothrombin values, the hippuric acid excretion test, the bromsulfalein excretion test, the cephalin-flocculation test, the tyrosine test, and the blood amylase test.<sup>25</sup> Somogyi<sup>26</sup> stated that remarkably low values were secured by the blood amylase test in persons with hepatic damage. In his own experience the test had many times directed attention to pathologic changes, later confirmed at autopsy before they were apparent clinically.

The Takata Ara reaction is reported to be useful in differentiating between intrahepatic carcinoma and extrahepatic carcinoma (of the bile ducts and pancreas) when jaundice is present. According to Stein,<sup>27</sup> the reading is negative in carcinoma of the pancreas and of the extrahepatic ducts without hepatic metastasis and positive in jaundice due to extensive primary carcinoma of the liver. In his experience the negative reaction was correct in 19 of 19 cases and the positive reaction correct in 9 of 10, which suggests that the test is of definite though limited value in the differential diagnosis of jaundice.

**Röntgenography**—Röntgenography may be extremely useful in primary carcinoma of the liver in revealing such suggestive findings as esophageal varices, hepatic enlargement, masses in the hepatic area with elevation and fixation of the diaphragm, and localized bulges in the diaphragm. Elevation of the diaphragm, without the pleural reaction seen in subdiaphragmatic abscess, was stressed as an important diagnostic sign by Hermouille Diaz and Sotomayor.<sup>28</sup> García Capurro<sup>29</sup> pointed out that hepatic tumors arising from the anterior border of the left lobe tend to cause anteroposterior displacement of the stomach while tumors arising elsewhere in the liver may cause displacement of the esophagus posteriorly and the left with resulting difficulties in the passage of food. Pomerans and his associates<sup>30</sup> suspected primary carcinoma of the liver when a selective barium residue is found at the lesser curvature of the stomach, near the left hepatic lobe.

Visualization of the liver by thorotrast is a useful procedure which is not, however, free from risk. Moreover thorotrast is a radioactive substance which, according to MacLellan and his associates,<sup>31</sup> may be capable of initiating malignant changes.

Röntgenograms of the chest should be made, to exclude possible metastases. Urography and perirenal insufflation of air should be carried out to exclude possible hypernephroma and the biliary tract should be visualized. Finally the



This type of hemorrhage usually occurs from a necrotic nodule projecting from the surface of the liver and is the result of erosion of a large hepatic vessel by the malignant growth.

In addition to its association with hepatic cirrhosis and other conditions which may play an etiologic role, primary carcinoma of the liver has been reported in association with diabetes mellitus,<sup>22, 23</sup> purpura,<sup>24</sup> and hypoglycemia.<sup>25</sup> In all reported cases of hypoglycemia, sufficient normal liver tissue remained to maintain normal liver function and normal glycogen storage.

Hansen and his associates<sup>26</sup> reported a case of primary carcinoma of the liver in a 10-year-old child in which marked hypemia was associated with extreme osteoporosis and great bony deformity. The authors explained the osteoporosis as due to defective retention of calcium and phosphorus by the osseous system. Since the food intake was adequate, and since no defect of absorption could be demonstrated, it was concluded that osseous metabolism, which in some way was bound up with liver function, was perverted in this way by the malignant growth. Wood<sup>24</sup> reported a case of generalized xanthomatosis associated with primary carcinoma of the liver in an infant. No similar cases seem to be on record.

#### DIAGNOSIS

The diagnosis of primary carcinoma of the liver is not a simple matter because, as has been pointed out, the clinical picture is not characteristic. Diagnosis is, however, of great urgency for the disease is so rapidly fatal that treatment must be instituted without delay if it is to be of any avail.

The procedures by which diagnosis can be made will be instituted only if it is constantly borne in mind that the disease may exist. Such symptoms, therefore, as abdominal pain and distention, loss of weight, dyspnea and edema of the ankles in the absence of cardiac disease, enlargement and tenderness of the liver and signs of portal cirrhosis should lead to the suspicion of carcinoma of the liver in all persons over the age of 40 years. In younger persons a palpable mass in the region of the liver should be regarded as neoplastic until it is proved not to be.

**Laboratory Studies.**—Laboratory studies should be carried out routinely for they may help to exclude other diseases of the hepatobiliary system, but they do not supply much useful diagnostic information. The white blood cell count will exclude leucemia and infectious states; in this series it ranged from 4,000 to 15,000 per cu mm. The red blood cell count usually reveals some degree of anemia, which is not usually severe. Hematocrit readings, or better blood volume estimates may give a truer picture. In this connection the studies on chronic shock by Clark and his associates<sup>27</sup> are of interest. They show that in malnourished patient with malignant disease a depleted blood volume often masks the presence of severe anemia.

Blood sugar estimations are unlikely to reveal hypoglycemia unless the liver is seriously disorganized by the malignant growth. If cirrhosis is suspected, serum protein determinations may be useful. In the Charity Hospital-Touro Infirmary series the serum protein values were normal or only slightly

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## DIFFERENTIAL DIAGNOSIS

It is possible to do little more than mention the various conditions from which primary carcinoma of the liver must be differentiated. The most important is carcinoma of the stomach with hepatic metastases, with carcinoma of the transverse colon, the left colon and the rectum next in importance. Differentiation is chiefly by roentgenography.

Primary carcinoma of the liver associated with jaundice must be differentiated from cholelithiasis, and carcinoma of the gall bladder, extrahepatic bile ducts, ampulla of Vater and pancreas. Echinococcus cysts of the liver which are sometimes associated with jaundice must also be differentiated. Cardiac conditions must be excluded in cases in which dyspnea, hepatomegaly, abdominal pain, and edema of the ankles are present. If fever is prominent, hepatic abscess must be considered. Serious intra-abdominal hemorrhage in carcinoma of the liver can usually be differentiated from other acute abdominal catastrophes only by exploration. Splenitis of the liver although extremely uncommon is a diagnostic possibility. Gumma of the liver which is usually confined to the left lobe should be considered. Hepatic cirrhosis is a possibility especially if the liver is small though it must also be considered if the liver is large and nodular. Esophageal varices associated with a large nodular liver may be due either to primary carcinoma of the liver or to cirrhosis; they are almost never present in association with secondary hepatic carcinoma.\*

Banti's disease especially in children may be manifested by jaundice, ascites, anemia, hematemesis and splenomegaly though, as Wentz and Kato suggested, the symptom complex might better be designated Banti's syndrome since it can occur in association with hepatic neoplasms. Benign tumors of the liver which are not uncommon in children, can be differentiated from hepatic malignancy only by histologic investigation.

In this series of cases of primary carcinoma of the liver the correct diagnosis was made only 13 times. In many reported series, cardiac disease with congestive failure was the most frequent diagnosis, being recorded 18 times. The clinical course of the disease is against the diagnosis, and although there may be marked edema of the feet jugular distention is not present. In Gregory's opinion the pedal edema is more marked in primary carcinoma of the liver than is compatible with a diagnosis of cardiac disease.

Other diagnoses included cirrhosis of the liver 13 times, carcinoma of the gastrointestinal tract, especially of the stomach, with hepatic metastases 10 times, anemias—which the patients did not have—6 times, carcinoma of the pancreas and gumma of the liver in 4 cases each, Hodgkin's disease in 3 cases, retroperitoneal sarcoma and carcinoma of the gall bladder 1 case each and in 1 case each Banti's syndrome, cerebral apoplexy, central nervous system syphilis, carcinoma of the lung, hydatid cyst of the liver, neuroendulatory asthenia, obstructive cholelithiasis, chronic leucemia, pancreatic cyst, hypernephroma, cystadenoma of the ovary and carcinoma of the extrahepatic biliary tract. Most of these diagnoses, it must be granted, did not seem unreasonable.

stomach and large bowel should be examined with an opaque medium to exclude carcinoma in those locations.

*Peritoneoscopy*—Peritoneoscopy which permits direct visualization of the liver has its greatest field of usefulness in differentiating between hepatic cirrhosis and hepatic malignancy. It is also of value if the clinical evidence is confusing, in determining operability in borderline cases, though the decision to withhold operation should be made with the greatest caution.

*Aspiration and Biopsy*—Aspiration of ascitic fluid, with microscopic examination sometimes reveals malignant cells. The method is therefore useful in distinguishing between a malignant process and hepatic cirrhosis or ascites due to cardiac disease though of course it furnishes no information as to the site of the malignancy. For best result the smear should be stained by the Papanicolaou technique.

The only entirely accurate and reliable diagnostic method is histologic examination of excised tissue which can be secured during peritoneoscopy by aspiration biopsy by punch biopsy or by surgical removal of specimen of liver at exploratory laparotomy. The chief objection to performing biopsy with peritoneoscopy is the inaccessibility of most tumors of the liver in addition to the fact that considerable specialized training and experience are necessary for the correct use of the instrument.

Opinions differ as to the value of aspiration biopsy. It is best indicated in the presence of superficial palpable masses apparently arising from the liver. Punch biopsy however is extremely valuable but it is by no means free from risk. Collected report covering 839 punctures indicate that the procedure was responsible for or contributed to, 10 deaths, or 1.2 per cent. Gillman and Gillman, who used a modification of the Iverson and Roholm apparatus, reported in 500 procedures one death from hemorrhage which is the most usual cause of fatalities. There were no deaths in their second 500 biopsies. By this method they were able to diagnose 11 cases of primary carcinoma of the liver in 42 cases of hepatomegaly due to various causes.

Volwiler and Jones<sup>20</sup> performed 234 biopsies with a mortality of 0.5 per cent. There were 4 hepatomas in their group each was diagnosed correctly by punch biopsy. The method is also useful when only a nodule can be palpated. It must be remembered, however that a negative biopsy is of no diagnostic value whatsoever since the specimen may not have been taken from a carcinomatous portion of the liver.

*Exploratory Laparotomy*—Exploratory laparotomy is entirely justified and indeed is strongly indicated as a diagnostic measure in any case in which the diagnosis cannot be made otherwise and in which suspicion of the disease cannot be positively excluded. The most satisfactory biopsy specimens are obtained when the abdomen is open and when at the same time the exact location, size, extent and gross characteristics of the tumor can be observed, local extension can be determined, and the possibility of metastases to regional lymph nodes or more distant structures can be evaluated. Exploration offers the patient with carcinoma of the liver his only chance of survival and there should be no hesitancy in resorting to it promptly.

and Clay.<sup>24</sup> The raw surface is then covered with the falciform ligament, while the right lobe is firmly attached to the diaphragm by figure-of-eight sutures.

None of the 50 patients reported in this communication were submitted to surgery. It seems fair to say that if the degree of clinical suspicion had been higher if exploration had been borne in mind as a diagnostic procedure and if it had been remembered that no patient with carcinoma of the liver has any chance of survival without surgery, the outcome in at least a few of these cases might have been different.

*Postoperative Complications*.—Possible postoperative complications include hemorrhage, hepatic abscess, peritonitis and ileus, respiratory complications, sinus formation with discharge of bile, hematemesis (from engorgement of the portal circulation as the result of clamping the hepatoduodenal vessels at operation) and such metabolic disturbances as liver shock, hepatic hypoglycemia and the hepatorenal syndrome. They are seldom troublesome. It is of interest that to date no case seems to have been reported in which the so-called liver death or hepatorenal syndrome occurred after resection of a primary carcinoma of the liver.

#### PROGNOSIS AND END RESULTS

All experience indicates that primary carcinoma of the liver is a rapidly fatal disease. Few patients live more than four to six months after the first clinical manifestation appears. In this series the duration of life from the onset of symptoms to death ranged from 4 days to 13 months and averaged 2.8 months. Eighty-two per cent of the patients were dead within 6 months, 61 per cent within 3 months, and 1 per cent within 1 month after they first became aware of the illness.

The incidence of metastases varied with the duration of life after the onset of symptoms. The more rapid the course the fewer the metastases. The average duration of life in 29 patients with liver cell carcinoma was 4.6 months and the incidence of metastases in this group was 93 per cent. Thirteen patients with lobular duct cell carcinoma lived on an average of 9.7 months after the onset of symptoms and presented an incidence of metastases of 69 per cent while the respective figures for five mixed cell tumors were 1 month and 40 per cent. These figures parallel those reported by Warr.<sup>25</sup> His 21 patients with hepatomas lived on an average of 5 months after the onset of symptoms, while in 9 patients with cholangiocarcinomas the duration of life was only 6 weeks.

Tinker and Tinker, Jr.<sup>26</sup> have properly pointed out that unfavorable results following partial resection of the liver for carcinoma are based upon the statistics of operations performed earlier in the century. Recent advances in preoperative and postoperative care, especially in respect to transfusion and other replacement therapy, improvements in anesthesia and surgical technique and the introduction of chemotherapy and antibiotic therapy have made hepatectomy like many other operations which were formerly extremely hazardous, reasonably safe procedures. There is general agreement that recurrences following operation can usually be attributed to inadequate removal of neoplastic tissue.

## THERAPY

The treatment of primary carcinoma of the liver is strictly surgical. In the presence of diffuse intrahepatic metastases the outlook is obviously hopeless, but in its absence surgical extirpation of the tumor should be attempted. Warrel,<sup>11</sup> in a review of the literature, compiled certain criteria which, in the opinion of many authorities, should be met before operation is carried out: (1) The carcinoma must be of the solitary localized variety. (2) There must be no evident lymph nodes, blood vessel or bile duct involvement at the hepatic hilum. (3) There must be no marked reduction of hepatic function. Other authorities, such as McArthur,<sup>12</sup> Cattell,<sup>13</sup> and Brunschwig<sup>14</sup> are far more radical and perform extensive resections of the liver even when adjacent organs are involved or secondary deposits are known to be present.

Certain anatomic and physiologic features of the liver are favorable to resection. The free anastomosis between the right and left hepatic arteries, as Martens<sup>15</sup> and Mann<sup>16</sup> emphasized, ensure that the blood supply will be adequate if one or the other is divided. Again the lobes and lobules are supplied by independent arteries, so that single areas may be removed without harmful consequences to the areas left in situ.

Mann's<sup>16</sup> extensive studies have shown that if the portal circulation is adequate and intact, restoration of hepatic tissue after partial hepatectomy is rapid and complete; in experimental animals as much as 80 per cent of the liver can be removed with safety. The same regeneration apparently occurs in human subjects, as Wendel<sup>14a</sup> demonstrated in 1930. He found an organ of approximately normal size when he operated for the second time on a woman whose liver he had partially resected two years earlier.

Resection of the liver for both benign and malignant neoplasms has been practiced for many years. Notable contributions were made by Keen,<sup>17</sup> Yeomans,<sup>18</sup> G. Turner,<sup>19</sup> Wright,<sup>20</sup> P. Turner,<sup>21</sup> Kidd<sup>22</sup> and Abel, and, more recently by Cattell,<sup>23</sup> Benson and Penberthy,<sup>24</sup> Packard and Stevenson,<sup>25</sup> Pickrell and Clay<sup>26</sup> and Wallace.<sup>27</sup> The experience with wounds of the liver in World War II furnishes further impetus to continued endeavors in the field of partial hepatectomy.

The chief difficulty encountered at operation is control of hemorrhage. Manipulation, electrocauterization, elastic tourniquets, packs, deep interlocking mattress sutures, and temporary clamping of the main blood supply have all been employed with varying degrees of success. A useful method of

— — — devised in 1933 by  
 nient modern coun-

ically simpler when the malignant tumor occupies other or those sites than is excision of only the carcinomatous area. Mobilization is accomplished by dividing the falciform ligament near its diaphragmatic attachment, while hemostasis is carried out with two or more rows of mattress sutures of braided silk or cotton placed in the interlobar sulcus and tied on the inferior surface, after the method of Packard

**Operation**—Operation was carried out August 9 by one of us (A. O.). The abdomen was opened through transverse upper abdominal incision. The only abnormal finding, after thorough search of all portions of the peritoneal cavity for possible primary site, was tumor mass measuring about 7 cm. in diameter in the left lobe of the liver. Frozen section confirmed the preoperative diagnosis of primary carcinoma (hepatic cell) of the liver. Resection of the left lobe was carried out. Through and through overlapping mattress sutures of chrome No. 1 catgut were passed through the lesser of the division between the lobes and were drawn tight but not tied. The left lobe of the liver with the tumor in situ, as resected with scalpel. The sutures already placed were then tied on the superior surface and additional sutures were placed at individual bleeding points. The raw surface was covered with the falciform ligament. The anterior abdominal wall closed in layers, with return of quilting cotton and No. 30 cotton. (Refer to Fig. 1.)

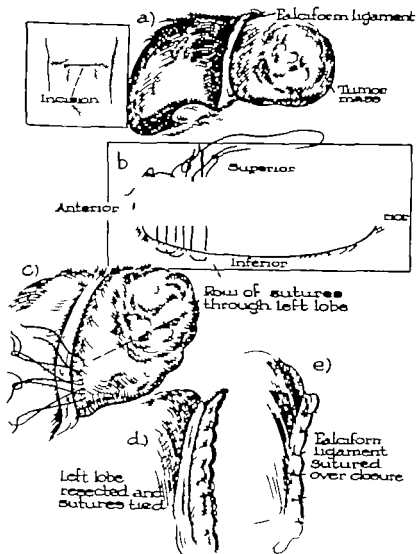


Fig. 1.—Diagram shows steps in performance of lobectomy.



The large number of resections of the liver collected from the literature by Warri<sup>42</sup> is not useful for the purposes of this communication because the distribution into benign and malignant cases is not entirely clear. Wallace<sup>43</sup> collected statistics, though the series is not large, can probably be assumed to be typical of present-day results. Of 29 patients with resectable hepatomas, 23 survived operation. Eight of 90 patient upon whom follow up studies were done were known to have recurrences, but 12 were known to be alive and well for periods ranging from two to five years after operation. Of 16 cases collected by Yeomans,<sup>44</sup> 4 patients died after operation, 6 developed recurrences at various times, but 6 were alive and well at intervals varying from three to seven years. When one considers that without surgery carcinoma of the liver is 100 per cent fatal even higher mortalities and even higher recurrence rates would not seem prohibitive. The statistics, in fact, warrant more frequent attempts at resection, removal of localized tumors, or complete lobectomy since surgery alone offers the patient the only chance for survival.

#### REPORT OF CASE

A 54-year-old white man as seen at the Out-patient Clinic July 14, 1947 with the chief complaints of indigestion and mass in the stomach. Four months earlier while taking usual (mammal) milk, he had sudden, severe, colicky pain in the epigastrium, which was

then he was again awakened from sleep by severe colicky epigastric pain. Again he was more comfortable in sitting position. This time the pain did not disappear completely for three or four days and during this attack he noticed for the first time small mass in the epigastrium.

Except for history of recent fatigue, especially during the three weeks before he was first seen, the patient had no other symptoms of any kind. He had lost no weight. Past

73 pounds, 10  
(the abdominal)  
was. Palpation

revealed it to be tender of firm consistency and slightly mobile. It moved on respiration. The pulsations of the aorta were readily transmitted through it. It seemed to be just beneath the anterior abdominal wall and was thought to be attached to the liver the edge of which was barely palpable. No other masses could be palpated in the abdomen.

**Laboratory Data.**—Urinalysis and blood serology were negative. The red blood cell count was 4,850,000 and the white blood cell count 9,000 per cu mm. The hemoglobin was 15 Gm per cent. The blood amylase was 55 mg per cent. The sedimentation rate was 4 mm in one hour. The cephalin flocculation test was 1 plus and the bromsulphalein excretion test showed 1 per cent retention in 45 minutes. The urea clearance test showed 73 per cent excretion in 2 hours. Stool examination showed *Giardia lamblia*. The glucose tolerance curve

was normal.

**Other Test.**—Roentgenologic examination of the chest, gall bladder and upper gastro-intestine was negative. The electrocardiogram

showed primary sinusoidal hemorrhage. The first attacks of pain were

The final diagnosis, carcinoma of the liver was confirmed by biopsy. The tumor explained on the basis of hemorrhage and the tumor

The subsequent postoperative course was relatively uneventful. The patient was allowed out of bed August 4 and was discharged in good condition three days later.

**Pathologic Report.**—The specimen, which consisted of the left lobe of the liver weighed 70 Gm. On its lower margin was a mass 5.5 by 6.5 cm. lobulated and faintly yellow. The surrounding parenchyma appeared normal (refer to Figs. 1 and 2).

Sections of the tumor showed numerous indistinct lobules of neoplastic cells which are compactly arranged and generally polygonal. Their nuclei were large, eosinophilic and hyper-

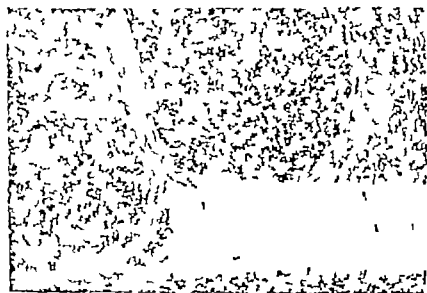


Fig. 1.—Photomicrograph showing interface (the edge) of tumor separated from hepatic tissue by compression push. (14 mm to 30 in and down, X140.)

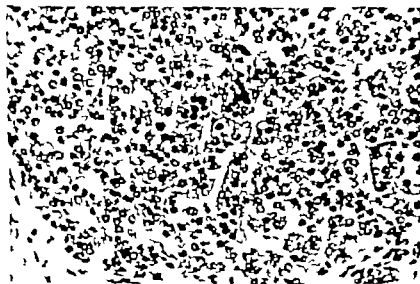


Fig. 2.—Photomicrograph showing high power view of tumor. (17 in. Hematoxylin and eosin, X400.)

The patient given 1,500 cc. of blood during the operation and was returned to the ward in good condition. Bleeding had been slight.

*Postoperative Course*—Six hours after operation the patient sustained complete wound disruption. Under general anesthesia and tubercurarine closure. Covered by through and through sutures of No. 10 rocket cotton placed at 2 cm. intervals. During the next 72 hours the abdomen became greatly distended with fluid, and on the fifth day after operation second wound disruption occurred. The wound again closed under general anesthesia in the same fashion after the first disruption.



Fig. 2.—Photograph of tumor and resected left lobe of liver



Fig. 3.—Photograph showing extent of tumor in resected left lobe of liver

The subsequent postoperative course was relatively uneventful. The patient, as allowed out of bed August 4, was discharged in good condition three days later.

**Pathologic Report**—The specimen, which consisted of the left lobe of the liver, weighed 530 Gm. On its lower margin was mass 55 by 63 cm, lobulated and faintly yellow. The surrounding parenchyma appeared normal (refer to Figs. 1 and 3).

Sections of the tumor showed numerous distinct lobules of neoplastic cells, which were compactly arranged and generally polygonal. Their nuclei were large, vesicular, and hyper-



Fig. 1.—Photomicrograph showing peripheral zone of tumor, characterized by compact, polygonal cells with large, vesicular nuclei, arranged in lobules (Hematoxylin and eosin, X100).



Fig. 2.—Photomicrograph showing inner zone of tumor, characterized by compact, polygonal cells with large, vesicular nuclei, arranged in lobules (Hematoxylin and eosin, X100).

chromatic. Mitosis was fairly frequent. The cytoplasm of the cells was granular. In some areas this trabeculation of fibrous tissue separated the tumor cells into discrete nests or cords (refer to Figs 4, 5, and 6).

The macroscopic diagnosis was primary liver cell carcinoma.

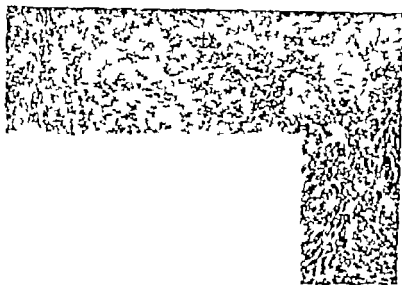


Fig. 6.—Photomicrograph showing trabeculae along edge of tumor poorly defined from hepatic tissue (Hematoxylin and eosin,  $\times 40$ ).

#### SUMMARY AND CONCLUSIONS

Against background of 5 histologically proved cases of primary carcinoma of the liver collected from two New Orleans hospitals, the disease has been discussed from the standpoint of incidence, etiology, clinical manifestations, pathology, diagnosis, and therapy.

The diagnosis of primary carcinoma of the liver is not easy because the clinical picture is not pathognomonic and is often vague and obscure.

The disease is rapidly fatal, the course without surgical treatment, being measured in months. Every possible diagnostic measure should therefore be employed, and exploratory laparotomy should be resorted to without delay if the suspicion of primary carcinoma of the liver is aroused and cannot positively be excluded otherwise. Surgery with complete excision of the tumor offers the only hope for survival, and should be undertaken without delay unless the case is clearly hopeless.

In view of the uniformly lethal outcome without surgery, the mortality and the rate of recurrence reported after operation do not seem unduly high.

An instance of successful resection of primary carcinoma of the liver is recorded.

In addition to the 5 autopsied cases of primary carcinoma of the liver reported in this communication 93 other cases of the disease were collected from the records of Charity Hospital. They were diagnosed by other methods in

cluding, in 28 cases, histologic examination of a biopsied specimen secured at exploratory laparotomy. These cases will be reported in another communication.

It is our pleasure to express our sincerest gratitude to Miss E. M. Petridge for her able criticism and help in the preparation of this publication.

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